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Form PTO-1390 (Modified) (REV 11-98) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371	29841/36636 BOX SEQ
	U.S. APPLICATION NO (IF KNOWN, SEE 37 CFR) 09/601667

AUG 0 3 2000

PATENT & TRADEMARK OFFICE

INTERNATIONAL APPLICATION NO	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP99/00696	03 February 1999	03 February 1998

TITLE OF INVENTION
Recombinant Mistletoe Lectins

533 Rec'd PCT/PTO 03 AUG 2000

APPLICANT(S) FOR DO/EO/US
Morris et al.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c) (2))
   a. ☒ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ A copy of the International Search Report (PCT/ISA/210).
8. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.
9. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
10. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
11. ☐ A copy of the International Preliminary Examination Report (PCT/IPEA/409).
12. ☐ A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 13 to 20 below concern document(s) or information included:

13. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
14. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
15. ☒ A **FIRST** preliminary amendment.
16. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
17. ☐ A substitute specification.
18. ☐ A change of power of attorney and/or address letter.
19. ☒ Certificate of Mailing by Express Mail
20. ☒ Other items or information: Diskette containing Sequence Listing; 1.821(f) Statement.

I hereby certify that this paper and the documents referred to as enclosed therewith are being deposited with the United States Postal Service on August 3, 2000, in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231 utilizing the "Express Mail Post Office to Addressee" service of the United States Postal Service under Mailing Label No. EM 099 903 511 US

Richard Zimmermann

U.S. APPLICATION NO (IF KNOWN, SEE 37 CFR	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/601667	PCT/EP99/00696	29841/36636

21. The following fees are submitted..

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :		CALCULATIONS PTO USE ONLY
☐ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2) paid to USPTO and International Search Report not prepared by the EPO or JPO	$970.00	
☒ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but Internation Search Report prepared by the EPO or JPO	$840.00	
☐ International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO	$690.00	
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4)	$670.00	
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4)	$96.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =		$840.00
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).		$0.00

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	49 - 20 =	29	x $18.00	$522.00
Independent claims	3 - 3 =	0	x $78.00	$0.00
Multiple Dependent Claims **(check if applicable)**.			☒	$260.00
TOTAL OF ABOVE CALCULATIONS			=	$1,622.00
Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28) **(check if applicable)**.			☐	$0.00
SUBTOTAL			=	$1,622.00
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).			+	$0.00
TOTAL NATIONAL FEE			=	$1,622.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3 31) **(check if applicable).**			☐	$0.00
TOTAL FEES ENCLOSED			=	$1,622.00
			Amount to be: refunded	$
			charged	$

☒ A check in the amount of **$1,622.00** to cover the above fees is enclosed.

☐ Please charge my Deposit Account No. in the amount of to cover the above fees.
A duplicate copy of this sheet is enclosed.

☒ The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. **13-2855** A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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NAME

36,107
REGISTRATION NUMBER

August 3, 2000
DATE

PATENT
Attorney Docket No.29841/36636

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE (PCT R/O)

Applicants:	)	Express Mail Certificate No.
	)	EM 099 903 511 US
Peter Morris, Thomas Stiefel,	)	
Wolfgang Voelter and Peter Welters	)	Dated: August 3, 2000
	)	
National Phase of PCT/EP99/00696	)	I hereby certify that this paper (or fee) is
Filed: 03 February 1999	)	being deposited with the United States
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Serial No. To be assigned	)	OFFICE TO ADDRESSEE" service under
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Filed: To be assigned	)	and is addressed to the BOX PCT,
	)	Assistant Commissioner for Patents,
For: RECOMBINANT	)	Washington, D.C. 20231.
MISTLETOE LECTINS	)	
	)	
Group Art Unit: To be assigned	)	Richard Zimmermann
	)	
Examiner: To be assigned	)	

PRELIMINARY AMENDMENT

BOX PCT
Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Prior to examination please amendment application as follows.

IN THE CLAIMS:

In claim 17, line 2, please delete "to 9" therefrom.

In claim 24, line 1, please delete "to 3" therefrom.

In claim 24, line 5, please delete "to 20 and "to 23" therefrom.

In claim 26, line 2, please delete "to 20" therefrom.

In claim 26, line 2, please delete "to 23" therefrom.

In claim 29, line 2, please delete "or 9" therefrom.

In claim 33, line 2, please delete "to 9" therefrom.

In claim 36, line 1, please delete "to 9" therefrom.

In claim 37, line 1, please delete "to 9" therefrom.

In claim 44, line 1, please delete "to 3 or 40 to 42" therefrom.

Respectfully submitted,

MARSHALL, O'TOOLE, GERSTEIN,
MURRAY & BORUN

By: _____

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August 3, 2000

Recombinant Mistletoe Lectins

526 Rec'd PCT/PTO 03 AUG 2000

The present invention relates to processes for the production of mistletoe lectin polypeptides in homologous and heterologous host systems and mistletoe lectin peptides as such. Further, nucleic acid molecules are provided, which code for these mistletoe lectin polypeptides, and also pharmaceutical compositions which contain these mistletoe lectin polypeptides or mistletoe lectin nucleic acids.

Mistletoe (Viscum album) has been known from antiquity as a healing plant. The semishrub plant lives as a semiparasite on the branches of woody plants and is particularly widespread in Europe, North Australia, Asia and in tropical and subtropical Africa. At the start of this century, the cyto- and tumour-toxic action of mistletoe extract, which has since then been specifically used for cancer therapy, was recognised. For this, the extract is used both as a single therapeutic agent and also in combination with chemo- or radiation therapy. Mistletoe preparations are particularly often used for example as a prophylactic against relapse after surgical tumour removal.

Systematic studies of the mode of action show that, after injection, aqueous mistletoe extract as well as its cytotoxic action also has an immunomodulatory effect, and apart from this shows generally mood-brightening effects. After injection of mistletoe extract, a significant increase in the cell numbers of certain lymphocyte subpopulations (inter alia T helper lymphocytes, natural killer (NK) cells and macrophages) and phagocytosis activity in granulo- and monocytes, which are directly involved in tumour defence, are observed (Hajto T, Hostanska K, Gabius H-J, (1990), Therapeutikum **4**, 135-145; Beuth J, Ko H L, Tunggal L, Gabius H-J, Steuer M, Uhlenbruck G, Pulverer G (1993), Med. Welt **44**, 217-220; Beuth J, Ko H L, Tunggal L, Geisel J, Pulverer G (1993), Arzneim.-Forsch/Drug Res. **43** (1), 166-169; Beuth J, Ko H L, Gabius H-J, Burricheter H, Oette Kl, Pulverer G (1992), Clin. Investing, **70**, 658-661). Further, a significant increase in defined acute phase proteins in the serum, which is mediated by the cytokines IL-1, IL-6 and TNF-α, can be detected (Hajto T, Hostanska K, Frei K, Rordorf C, Gabius H-J (1990), Cancer Res. **50**, 3322-3326; Beuth J, Ko H-L, Gabius H-J, Pulverer G (1991), In Vivo **5**, 29-32; Beuth J, Ko H-L, Tunggal L, Jeljaszewicz J, Steuer M K, Pulverer G (1994), In Vivo **8**, 989-992; Beuth J, Ko H-L, Tunggal L, Jeljaszewicz J, Steuer

M K, Pulverer G (1994), Dtsch. Zschr. Onkol. **26**, 1-6; Beuth J, Ko H-L, Tunggal L, Steuer M K, Geisel J, Jeljaszewicz J, Pulverer G (1993), In Vivo 7, 407-410; Kayser K, Gabius S, Gabius H-J, Hagemeyer O (1992) Tumordiag. und Ther. **13**, 190-195). As well as the prolongation of the survival time of cancer patients achievable by mistletoe extract treatment, an increase in the patients' quality of life is also observed, which is attributed to the rise in β-endorphins in the blood (Heiny B-M, Beuth J (1994), Anticancer Res. **14**, 1339-1342; Heiny B-M, Beuth J (1994), Dtsch. Zschr. Onkol. **26**, 103-108). As endogenous opioids, β-endorphins improve the general well-being, in that they for example have a pain-relieving action, and improve the pain index (Falconer J, Chan E C, Madsens G (1988), J. Endocrinol. **118**, 5-8).

Analysis of the active substances of mistletoe extract has shown that the immunostimulating effect is attributable to a certain group of glycoproteins, the mistletoe lectins. Hitherto, three mistletoe-specific lectins with different molecular weights and sugar-binding specificities had been identified. The concentration of mistletoe lectin I (ML-I) in the aqueous plant extract is markedly higher than that of mistletoe lectin II (ML-II) and mistletoe lectin III (ML-III). It could be shown that the immunostimulating effect of the mistletoe extract is attributable to the presence of ML-I: if the ML-I lectin is removed from the mistletoe extract, the extract loses its immunostimulating action (Beuth J, Stoffel B, Ko H-L, Jeljaszewicz J, Pulverer G (1995), Arzneim.-Forsch./Drug. Res. **45** (II), 1240-1242). The β-galactoside-specific ML-I lectin consists of two A- and two B-chains (MLA and MLB), each glycosylated, whose molecular weights are about 29 kDa and 34 kDa respectively. The amino acid sequence of MLA contains one potential glycosylation site, while MLB contains three glycosylation sites in the N-terminal region of the amino acid sequence. The two chains are linked together via a disulphide bridge (Figure A; Ziska P, Franz H, Kindt A (1978), Experientia **34**, 123-124). The resulting mistletoe lectin monomers can associate into dimers with the formation of non-covalent bonds.

Studies of the sedimentation behaviour of ML-I during analytical centrifugation show that in vivo ML-I is present in a monomer-dimer equilibrium (Luther P, Theise H, Chatterjee B, Kardruck D, Uhlenbruck G (1980), Int. J. Biochem. **11**, 429-435). The MLB-chain is able to bind to galactose-containing structures on the surface of cell membranes (e.g. receptor

molecules) and thereby to trigger cytokine release. Through endocytosis, ML-I dimers and monomers get into the cell, where the protein complexes break down into MLA and MLB chains through reduction of the disulphide bridge bonds. The MLA chains are thereupon able to bind to the ribosomal 28 S subunit and to inactivate this.

The study of ML-I monomers using 2-D gel electrophoresis yielded 25 different isoforms, which are attributable to different combinations of various A and B chains and different glycosylation states of the chains (Schink et al., 1992, Naturwissenschaften **79**, 80-81). It is suspected that the individual isoforms fulfil specific functions and each of these isoforms contributes to the anti-tumorigenic effect of the mistletoe extract.

By now, a nucleic acid sequence and the amino acid sequence derived therefrom of one ML-I lectin is already known from European Patent Application EP 0 751 211 A1. However this one polypeptide is not capable of satisfactorily emulating the action of the many ML-I isoenzymes contained in natural mistletoe extract as regards the anti-tumorigenic and mood-brightening effect.

Hence the technical problem of the present invention is to provide a process which makes it possible to produce mistletoe lectins in sufficient quantities and at the same time to imitate the diversity in ML-I isoenzymes of the natural mistletoe extract.

The problem is solved according to the invention by the provision of a process according to Claim 1 and/or 40.

The present invention moreover makes available 2 new polypeptides of the MLA chain and 6 new polypeptides of the MLB chain of ML-I, which can be expressed individually or in combination in a suitable host system. Thereby, "homologous" and "heterologous" ML-I dimers are formed, where the term "homologous" denotes a dimer which consists either of two MLA and two MLB chains, each the same and the term "heterologous" denotes a dimer which consists of two different MLA and/or two different MLB chains. The diversity of the MLA and MLB chains makes it possible to create a multitude of different MLA/MLB complexes, the therapeutic action of which is modelled on the above-described action of the

lectin mixture which was detected in aqueous mistletoe extract. One of the advantages which the present invention offers compared to the conventional extraction of mistletoe extracts from fresh plants is that the immunomodulating components of the mistletoe extract can be produced by a biotechnological process. This means that sufficient quantities of mistletoe lectin I can be produced independently of plant material, which is only available to a limited extent and can only be harvested at a certain time of year. Furthermore, a mixture of mistletoe lectins biotechnologically produced in this way contains none of the "impurities" occurring in the natural mistletoe extract, e.g. viscotoxins.

Further, owing to the fact that the present invention makes a large number of different MLA and MLB polypeptides of ML-I available, it becomes possible to "design" pharmacological compositions in a target-oriented manner. This means that e.g. by the selection of certain MLB polypeptides which define the binding affinity of the MLA/MLB complex to the target cells, the immunomodulatory action of a composition can be influenced. Furthermore, by the use of defined MLA polypeptides, the cytotoxicity of a composition can be varied.

In order to be able biotechnologically to produce the mixture of mistletoe lectins contained in mistletoe extracts, firstly the amino acid sequence of a pharmaceutically interesting mistletoe lectin was elucidated. For this, a mistletoe extract was obtained from *Viscum album L. ssp. platyspermum* Kell, which were harvested from poplars, and mistletoe lectin I was partially purified by affinity chromatography (Example 1). The subsequent analysis by SDS-PAGE, HPLC and sequence analysis by Edman degradation showed 2 MLA isoforms and 6 MLB isoforms.

Degenerate oligonucleotides were derived from short regions of the amino acid sequences, and by means of these the genomic mistletoe lectin I DNA sequence was determined using the PCR process. Surprisingly, in spite of the many identified ML-I amino acid sequences, only a single nucleic acid sequence more less corresponding to these sequences was identified. By Southern blot analysis, it was confirmed that the ML-I gene occurs in only one copy per genome. Hence the sequence variability of the MLA and MLB polypeptides is to be explained only by the occurrence of RNA editing or other posttranscriptional or posttrans-lational modifications in mistletoe cells.

All processes that lead to differences between the final mRNA sequence and the corresponding "template" DNA, except for "RNA-splicing" and tRNA modifications, are described as "RNA-editing". "mRNA-splicing", and also the occurrence of modified tRNAs, is generally known and is therefore not explained in more detail here. In "RNA-editing", individual nucleotides or strands of up to several hundred nucleotides in length are exchanged, inserted or deleted co- or posttranscriptionally, which can lead to reading-frame changes in the coded sequence. The first example of RNA-editing was discovered in studies of the coxII transcript of the mitochondrial DNA of trypansomes (Benne R et al (1986) Cell **46**, 819-826). Further, this process has been detected in mitochondria and chloroplasts of higher plants and singular nuclear transcripts in mammalian cells. The precise mechanism of RNA editing, like the mechanisms for posttranslational modifications of the primary amino acid sequence have however so far only been very incompletely described in the literature.

Since however this process has so far only been detected in very few plants and the aim is to make biotechnological production of the various mistletoe lectin I polypeptides also possible in other plant cells than mistletoe cells as far as possible independently of posttranscriptional or posttranslational changes, the genomic DNA was matched to the sequence of the various isolated polypeptides by deliberate mutations. Furthermore, the genomic sequence was matched to the preferred codon utilisation of *Brassica*, in order to make optimal expression possible e.g. in rape cells.

Hence the present invention makes available a process for the production of a mistletoe lectin polypeptide or a fragment thereof in the heterologous system having the following sequence:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S D V R Y W P L V I R P V I A D D

V T C S A S E P T V R I V G R X21 G M X22 V D V

R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I

W X24 N G T I I N P R S N L V L A A S S G I K G

T T L T V Q T L D Y T L G Q G W L A G N D T A

P R E V T I Y G F R D L C M E S N X25 G S V W V

E T C X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R

P K Q N Q D Q C L T X30 G R D S V S T V I N I V

S C S X31 X32 S X33 X34 Q R W V F T N E X35 A I L N

L K X36 X37 X38 X39 X40 D V A Q A N P K L R R I I I

Y P A T G K P N Q M W L P V X41

including the step of expressing of a eukaryotic or prokaryotic vector, into which a nucleic acid coding for the mistletoe lectin polypeptide according to the usual genetic code or a fragment thereof is cloned, in a suitable heterologous eukaryotic or prokaryotic host,

wherein X1 is D or E, X2 is G or Q, X3 is I or V, X4 is L or A, X5 is DR or missing, X6 is N or T, X7 is P or T, X8 is D or E, X9 is S or T, X10 is F or Y, X11 is T or A, X12 is A or Y, X13 is Y or D, X14 is A or E, X15 is V or M, X16 is I or F, X17 is P or S, X18 is P or T, X19 is T or S, X20 is D or S, X21 is N or S, X22 is C or R, X23 is G or N, X24 is G or D,

X25 is G or Q, X26 is V or D, X27 is Q or K, X28 is G or missing, X29 is R or K, X30 is C or S or V, X31 is A or G, X32 is G or A, X33 is S or G, X34 is G or S, X35 is G or Y, X36 is N or S or T or K, X37 is S or G, X38 is L or P, X39 is A or M, X40 is M or V and X41 is P or F.

Analogously to this process, two further production processes for the mistletoe lectin A-chain (MLA) and mistletoe lectin B-chain (MLB) are made available, which contain the following sequences or a fragment thereof:

Mistletoe Lectin A:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S

Mistletoe Lectin B:

D D V T C S A S E P T V R I V G R X21 G M X22 V D

V R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I W

X24 N G T I I N P R S N L V L A A S S G I K G T T

L T V Q T L D Y T L G Q G W L A G N D T A P R E

V T I Y G F R D L C M E S N X25 G S V W V E T C

X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R P K Q N

Q D Q C L T X30 G R D S V S T V I N I V S C S X31

X32 S X33 X34 Q R W V F T N E X35 A I L N L K X36 X37

X38 X39 X40 D V A Q A N P K L R R I I I Y P A T G

K P N Q M W L P V X41

wherein X1 to X41 have the meaning stated above.

Furthermore, a mistletoe lectin polypeptide or a fragment thereof, which includes the sequence variability of the various MLA and MLB chains, having the following sequence is provided:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S D V R Y W P L V I R P V I A D D

V T C S A S E P T V R I V G R X21 G M X22 V D V

R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I

W X24 N G T I I N P R S N L V L A A S S G I K G

T T L T V Q T L D Y T L G Q G W L A G N D T A

P R E V T I Y G F R D L C M E S N X25 G S V W V

E T C X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R

P K Q N Q D Q C L T X30 G R D S V S T V I N I V

S C S X31 X32 S X33 X34 Q R W V F T N E X35 A I L N

L K X36 X37 X38 X39 X40 D V A Q A N P K L R R I I I

Y P A T G K P N Q M W L P V X41

Apart from this, mistletoe lectin polypeptides of the mistletoe lectin A-chain and mistletoe lectin B-chain or fragments of these sequences are provided, which include the following sequences:

Mistletoe Lectin A:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S

Mistletoe Lectin B:

D D V T C S A S E P T V R I V G R X21 G M X22 V D

V R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I W

X24 N G T I I N P R S N L V L A A S S G I K G T T

L T V Q T L D Y T L G Q G W L A G N D T A P R E

V T I Y G F R D L C M E S N X25 G S V W V E T C

X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R P K Q N

Q D Q C L T X30 G R D S V S T V I N I V S C S X31

X32 S X33 X34 Q R W V F T N E X35 A I L N L K X36 X37

X38 X39 X40 D V A Q A N P K L R R I I I Y P A T G

K P N Q M W L P V X41

wherein X1 to X41 have the meaning stated above.

The sequence which includes the above-described variability of the ML-I polypeptides occurring in mistletoe cells is shown in Figure 1b. A specific sequence for MLA2 of mistletoe lectin I, which was likewise produced according to the process presented above, is shown in Figure 3b. Figures 7b to 12b include specific mistletoe lectin B-chain sequences, which were likewise produced according to the process described above.

A further aspect of the present invention is a process for the provision of a nucleic acid molecule, which codes for a mistletoe lectin polypeptide in a heterologous host as described above and includes the following steps:

a) preparing of mistletoe cell RNA or chromosomal mistletoe cell DNA and

b) amplifying mistletoe cell RNA or chromosomal mistletoe lectin DNA by PCR using oligonucleotides which are derived from the mistletoe lectin polypeptide shown in Fig. 1b, and

c) if necessary, identifying of sequences which lie 5' and 3' from the amplified nucleic acid and amplification thereof, and

d) isolating of the nucleic acid molecules amplified in step b) and/or c), and

e) if necessary, ligating of several of the nucleic acid molecules amplified in step b) and/or c), such that a nucleic acid molecule with a complete open reading frame is obtained and

f) targeted mutation of the nucleic acid molecule obtained in order to match the nucleic acid molecule to the usual genetic code of the heterologous host for one of the mistletoe lectin polypeptide isoforms identified in mistletoe cells.

For the preparation of mistletoe cell DNA, mistletoe plants (*Viscum album L. ssp. platy-spermum* Kell), which had been harvested from poplars from Alsace, were crushed in liquid nitrogen and the chromosomal DNA extracted (Example 1). Using the degenerate oligo-nucleotides shown below, fragments of the genomic mistletoe lectin DNA were amplified by means of the PCR process (Example 2). The degenerate oligonucleotides used in the PCR reaction, which hybridise to regions of the MLB chain DNA, have the sequence:

(BI):

GTN MGN GAY GAY GAY TTY CA

(BII):

AT YTG RTT NGG YTT NCC NGT

The abbreviations of the nucleotides here are based on the designation proposed by the IUPAC-IUB Biochemical Nomenclature Commission.

In a further reaction step, using specific oligonucleotides, the 5'- and 3'-lying sequences of the first amplification product were determined by means of the RACE technique (Example 3). The oligonucleotide used for the 5'-RACE reaction has the following sequence:
CAC AGC AGT ATT ACA GTC GAA.

The oligonucleotide used for the 3'-RACE reaction has the following sequence:
GTC TAT GTG ATG ATC TTC GAC TGT.

The complete nucleic sequence thus obtained was used for the synthesis of specific oligonucleotides in order to obtain a whole clone by means of the PCR. Alternatively, the partly overlapping clones were cleaved using suitable restriction cleavage sites, in order to be assembled in a suitable vector, so that a complete open reading frame of the mistletoe lectin I gene was obtained. Deliberate mutations can be introduced into these DNA constructs by known techniques, e.g. by replacement of certain DNA regions by other DNA fragments, introduction of not completely homologous oligonucleotides, etc. These mutations can serve on the one hand to modify the amino acid sequence derived therefrom and thus to influence the activity of the polypeptide, or on the other hand to vary the nucleic acid sequence, without modifying the amino acid sequence, in order e.g. to imitate the preferred codon usage of a host organism.

Nucleic acid molecules which are made available by this process and code for a polypeptide as described above, include the following sequences for ML-I, MLA and MLB or fragments thereof:

1) ML-I Sequence

TACGAGAGGCTAAGACTCAGAGTTACGCATCAAACCACGGGCGAKGAATACTTCCGGTTCATCACG

CTTCTCCGAGATTATGTCTCAAGCGGAAGCTTTTCCAATGAGATACCACTCTTGCGTCAGTCTACG

ATCCCCGTCTCCGATGCGCAAAGATTTGTCTTGGTGGAGCTCACCAACCAGGGGSRRGACTCGRTY

ACGGCCGCCATCGACGTTACCAATSYKTACGTCGTGGCTTACCAAGCAGGCGACCAATCCTACTTT

TTGCGCGACGCACCACGCGGCGCGGAAACGCACCTCTTCACCGGCACCACCCGAZ1TCCTCTCTCC

CATTCAMYGGAAGCTACMCYGATCTGGAGCGATACGCCGGACATAGGGACCAGATCCCTCTCGGTA

TAGASCAACTCATTCAATCCGTCWCKGCGCTTCGTTWYCCGGGCGGCAGCACGCGTRCYCAAGCTC

GTTCGATTTTAATCCTCATTCAGATGATCTCCGAGGCCGCCAGATTCAATCCCATCTTATGGAGGK

MYCGCCAAKAYATTAACAGTGGGGMRTCATTTCTGCCAGACRTGTACATGCTGGAGCTGGAGACGA

GTTGGGGCCAACAATCCACGCAAGTCCAGCATTCAACCGATGGCGTTTTTAATAACCCAWTYCGGT

TGGCTATAYCYMCYGGTAACTTCGTGACGTTGWCYAATGTTCGCKMYGTGATCGCCAGCTTGGCGA

TCATGTTGTTTGTATGCGGAGAGCGGCCATCTTCCTCTGACGTGCGCTATTGGCCGCTGGTCATAC

GACCCGTGATAGCCGATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAA

RTGGCATGYGCGTGGACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCT

CCAAGTCCAACAATGATCCGAATCAGTTGTGGACGATCAAAAGGGATRRMACCATTCGATCCAATG

GCAGCTGCTTGACCACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTG

CTGTGCGGGAGGCCACTATTTGGCAGATATGGGRCAATGGGACCATCATCAATCCAAGATCCAATC

TGGTTTTGGCAGCATCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTACACGT

TGGGACAGGGCTGGCTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGTTTCAGGG

ACCTTTGCATGGAATCAAATSRAGGGAGTGTGTGGGTGGAGACGTGCGWSAGTAGCCAAMAGAACC

AAZ2ARATGGGCTTTGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAAGACCAATGCCTCAC

CKBTGGGAGAGACTCCGTTTCAACAGTAATCAATATAGTTAGCTGCAGCGSWGSWTCGKSKKSKCA

GCGATGGGTGTTTACCAATGAAKRSGCCATTTTGAATTTAAAGAVWRGSYYGRYSRTGGATGTGGC

GCAAGCAAATCCAAAGCTCCGCCGAATAATTATCTATCCTGCCACAGGAAAACCAAATCAAATGTG

GCTTCCCGTGYYMTGA

II) MLA Sequence

TACGAGAGGCTAAGACTCAGAGTTACGCATCAAACCACGGGCGAKGAATACTTCCGGTTCATCACG

CTTCTCCGAGATTATGTCTCAAGCGGAAGCTTTTCCAATGAGATACCACTCTTGCGTCAGTCTACG

ATCCCCGTCTCCGATGCGCAAAGATTTGTCTTGGTGGAGCTCACCAACCAGGGGSRRGACTCGRTY

ACGGCCGCCATCGACGTTACCAATSYKTACGTCGTGGCTTACCAAGCAGGCGACCAATCCTACTTT

TTGCGCGACGCACCACGCGGCGCGGAAACGCACCTCTTCACCGGCACCACCCGAZ1TCCTCTCTCC

CATTCAMYGGAAGCTACMCYGATCTGGAGCGATACGCCGGACATAGGGACCAGATCCCTCTCGGTA

TAGASCAACTCATTCAATCCGTCWCKGCGCTTCGTTWYCCGGGCGGCAGCACGCGTRCYCAAGCTC

GTTCGATTTTAATCCTCATTCAGATGATCTCCGAGGCCGCCAGATTCAATCCCATCTTATGGAGGK

MYCGCCAAKAYATTAACAGTGGGGMRTCATTTCTGCCAGACRTGTACATGCTGGAGCTGGAGACGA

GTTGGGGCCAACAATCCACGCAAGTCCAGCATTCAACCGATGGCGTTTTTAATAACCCAWTYCGGT

TGGCTATAYCYMCYGGTAACTTCGTGACGTTGWCYAATGTTCGCKMYGTGATCGCCAGCTTGGCGA

TCATGTTGTTTGTATGCGGAGAGCGGCCATCTTCCTCT

III) MLB Sequence

GATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAARTGGCATGYGCGTG

GACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCTCCAAGTCCAACAAT

GATCCGAATCAGTTGTGGACGATCAAAAGGGATRRMACCATTCGATCCAATGGCAGCTGCTTGACC

ACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTGCTGTGCGGGAGGCC

ACTATTTGGCAGATATGGGRCAATGGGACCATCATCAATCCAAGATCCAATCTGGTTTTGGCAGCA

TCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTACACGTTGGGACAGGGCTGG

CTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGTTTCAGGGACCTTTGCATGGAA

TCAAATSRAGGGAGTGTGTGGGTGGAGACGTGCGWSAGTAGCCAAMAGAACCAAZ2ARATGGGCTT

TGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAAGACCAATGCCTCACCKBTGGGAGAGACT

CCGTTTCAACAGTAATCAATATAGTTAGCTGCAGCGSWGSWTCGKSKKSKCAGCGATGGGTGTTTA

CCAATGAAKRSGCCATTTTGAATTTAAAGAVWRGSYYGRYSRTGGATGTGGCGCAAGCAAATCCAA

AGCTCCGCCGAATAATTATCTATCCTGCCACAGGAAAACCAAATCAAATGTGGCTTCCCGTGYYMT

GA

The nucleotides are defined in accordance with the IUPAC-IUB code; Z_1 designates the nucleotide sequence GAT AGA or is missing, while Z_2 designates the nucleotide GGC or is missing.

A specific nucleic acid molecule which was prepared by the process stated above and includes the entire ML-I coding sequence, is shown in Figure 1a. Further specific nucleic acid molecules, which code for the MLA chain of mistletoe lectin I and were prepared by the process stated above, are shown in Figure 2a and Figure 2b. Specific sequences for MLB nucleic acid molecules, which were prepared by the process described above, are listed in

Figures 7a to 12 a. Here, each of these nucleic acid sequences codes for a polypeptide which emerged by protein sequencing of the ML-I mixture from natural mistletoe extract.

In addition, the present invention includes nucleic acid molecules which code for a mistletoe lectin polypeptide, as described above, and are characterised in that the codon usage is matched to the requirements of a heterologous host. Figure 4a shows such a nucleic acid sequence, wherein the codon usage is matched to the preferred codon usage of the genus *Brassica*. This genus was chosen, since both as the Summer and also as the Winter form it thrives outstandingly in the middle latitudes of Europe, North America and Asia. The possible uses of rape for the production of recombinant proteins have been demonstrated by various firms and research institutes. Examples of its use are the production of gastric lipase for use in the treatment of cystic fibrosis or coupling to oleosins for greater ease of purification of the recombinant proteins from the lipid phase of the rape oil seeds.

The sequences shown in Figures 5a, 6a and 13a to 18a represent nucleic acid molecules which code for MLA polypeptides or for MLB polypeptides of mistletoe lectin I and whose codon usage is likewise matched to the genus *Brassica*. The degree of homology between these matched sequences to the nucleic acid sequences shown in Figs. 2a and 7a is ca. 61% for MLA and about 63% for MLB.

Further, through the present invention a vector is made available, which includes one of the nucleic acid molecules described above or a fragment thereof and also a promoter regulating the expression of this nucleic acid molecule. In a preferred embodiment, this vector contains, in functional linkage with the nucleic acid molecules described above, a promoter which can only be activated in the intended host cell. The host cell here can be a plant or an animal cell. Host-specific promoters are already used, sometimes together with cell type-specific, regulated enhancer sequences, for the selective expression of therapeutic genes (Walter W and Stein U, Molecular Biotechnology, 1996, **6** (3), 267-86). Likewise, systems have been developed, wherein inducers and repressors act on a genetically modified transcription factor, which specifically recognises a likewise modified promoter. This allows the regulated expression of e.g. therapeutic proteins, without at the same time non-specifically activating cellular promoters (Miller N and Whelan J, Human Gene Therapy, 1997, **8** (7), 803-815).

A preferred vector is an RNA vector, such as for example described in Kumagai et al., Proc. Natl. Acad. Sci., USA, 1993, **90**, 427-430. Compared to other plant expression systems, this system offers the advantages firstly that high yields of recombinant proteins can be achieved and secondly a considerably faster establishment of the process takes place, since only the RNA vector is genetically modified, and after infection the plant starts the production of the recombinant protein.

Host systems which are to serve for the heterologous expression of the nucleic acids described above can be selected from the group including bacterial cells, plant cells with the exception of mistletoe cells, insect cells, insect larvae, vertebrate cells, preferably mammalian cells, yeast cells, fungal cells, transgenic vertebrates with the exception of man and/or transgenic plants with the exception of mistletoe plants. Here preferably *Escherichia coli* are used as bacterial cells, rape cells as plant cells, Trichoplusia ni as insect larvae, *Spodoptera frugiperda* cells as insect cells and zebra fish as vertebrates.

The present invention includes pharmaceutical compositions which contain at least one of the aforementioned nucleic acid molecules or one of the vectors described above.

A preferred pharmaceutical composition in addition contains liposomes, which enclose the linear nucleic acid molecules or the vectors, in order to protect them against nucleolytic degradation. At the same time, these liposomes can bear cell recognition molecules on their surface, which enable selective attachment to specific target cells. Such so-called "second generation" surface-modified liposomes (e.g. immunoliposomes and "long-circulating liposomes") are already being successfully used for the targeted transfection of specific cell types from cancer patients (Storm G and Crommelin D J, Hybridoma, 1997, **16** (1), 119-125, Thierry A R et al., Gene Therapy, 1997, **4** (3), 226-237).

A further pharmaceutical composition is specified, wherein the linear nucleic acid molecule or the vector is coupled directly or via a linker system (e.g. biotin-streptavidin coupling) to one of the MLB polypeptides described above. Here the MLB polypeptide unit mediates the attachment of the complex to sugar-containing structures on the cell membrane and induces the endocytotic uptake of the complex. In this way, for example a nucleic acid coding for the

cytotoxic MLA can be specifically transported into a cell, where it is subsequently translated into a protein and then inactivates the cell's own ribosomes. In addition, such a complex can contain peptides such as for example antibodies, antibody fragments or receptor-binding peptides (ligands), which are capable of effecting cell-specific binding.

A further preferred pharmacological composition includes a virus particle, as well as the linear nucleic acid molecule or the vector. In this case, a virus vector is preferred. Here the virus particle can likewise on its surface bear cell recognition molecules for specific cell recognition. These molecules can be e.g. fusion proteins of viral proteins with cell-specific-ally binding polypeptides. By presentation of these peptides on the surface of the virus particle, a targeted attachment of these particles can be achieved (Joelson T et al., Journal of General Virology, **78** (6), 1213-1217, Grabherr R et al., Biotechnics, 1997, **22** (4), 730-735).

The present invention further includes a pharmaceutical composition which contains at least one of the mistletoe lectin polypeptides described above and/or at least one fragment thereof as cytotoxic component. The pharmaceutical efficiency of such a composition can once again be heightened by coupling of the polypeptides or the polypeptide fragments with cell recognition molecules which bind selectively to target cells. In a preferred embodiment of the pharma-ceutical composition, the cell recognition molecule is an antibody molecule, an antibody fragment or any other protein and peptide molecule, which has the capacity specifically to bind to the target cells, e.g. a peptide hormone or a fragment of this hormone such as the "gonadotropin-releasing hormone" and such fragments which specifically bind to receptors of adenocarcinoma cells or peptides which in a specific form of leukaemia bind to the inter-leukin-2 growth factor of the lymphoma cells ("cutaneous T cell lymphoma"). Non-protein molecules which concentrate in target cells or bind to them, such as cis-platin or haem and precursors thereof, can be also suitable cell recognition molecules for coupling to the cyto-toxic component of the ML-I. Owing to the fact that the cytotoxic component specifically gets into the cell interior of the degenerated cells, the dose of toxin can be kept relatively low and side-effects on healthy tissue minimised.

Here these cell recognition molecules can be coupled to the mistletoe lectin polypeptides by known chemical processes. Furthermore, it is possible to create fusion proteins from the

polypeptides described above and a suitable antibody or a fragment thereof in one of the host systems likewise described above. Also suitable as fusion proteins are e.g. recombinant proteins which consist of a polypeptide described here and an IL-2 receptor-binding "homing" component or a genetically modified fragment of gonadotropin-releasing factor.

A pharmaceutical composition according to the invention contains at least one of the polypeptides described above and/or a fragment thereof, as a rule together with a pharmaceutically compatible vehicle. Here a defined mixture of different MLA and/or MLB polypeptides corresponding to the needs of the patient can be composed. In order to recreate the diversity of the mistletoe lectin I isoenzyme of natural mistletoe extract, a cytotoxic composition preferably contains several or all of the above-stated MLA/MLB polypeptides. The pharmaceutically tolerable carrier can be a buffer, a diluent, a filler, solvent, lubricant, flavouring, binder, preservative and/or occluding material. The pharmaceutical composition is formulated such that it is suitable both for oral and also parenteral administration, in particular subcutaneous, intramuscular and intravenous administration. In certain diseases, inhalational, rectal, vaginal and cutaneous presentations can also be used.

On account of an anti-tumorigenic action, an above-mentioned mistletoe lectin polypeptide or a fragment thereof can be used for production of a medicament for treatment of uncontrolled cell growth, e.g. of cancer. Furthermore, such a mistletoe lectin polypeptide or a fragment thereof, whose cytotoxic activity has been blocked, e.g. by modifications at the active centre (amino acids Y_{76}, Y_{115}, E_{165}, R_{168}, W_{199}), in combination with at least one further antigen, can be used for the production of a medicament, which is capable of intensifying the immune reaction against the further antigen. For example, from European Patent 0 320 528, proteins are already known (haemocyanins and arylphorins), which can cause a strong antigenic reaction. Similarly to these substances, the mistletoe lectins according to the invention can also trigger an activation of T-lymphocytes and lymphokine-producing macrophages and as a result strengthen the endogeneous defences.

Furthermore, the present invention also includes a process for the production of a mistletoe lectin polypeptide in mistletoe cells and/or transgenic mistletoe plants having the following sequence:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S D V R Y W P L V I R P V I A D D

V T C S A S E P T V R I V G R X21 G M X22 V D V

R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I

W X24 N G T I I N P R S N L V L A A S S G I K G

T T L T V Q T L D Y T L G Q G W L A G N D T A

P R E V T I Y G F R D L C M E S N X25 G S V W V

E T C X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R

P K Q N Q D Q C L T X30 G R D S V S T V I N I V

S C S X31 X32 S X33 X34 Q R W V F T N E X35 A I L N

L K X36 X37 X38 X39 X40 D V A Q A N P K L R R I I I

Y P A T G K P N Q M W L P V X41

comprising the step of expressing a eukaryotic vector, which contains a nucleic acid coding for the mistletoe lectin polypeptide or a fragment thereof having the nucleic acid sequence originally found in mistletoe cell DNA, in a mistletoe cell or a transgenic mistletoe plant, wherein the transcription product of this nucleic acid molecule is modified in mistletoe cells or transgenic mistletoe plants by RNA editing and further normally occurring postranscript-ional and/or posttranslational mechanisms and thus possibly leads to the production of the natural mistletoe lectin mixture,

wherein X1 is D or E, X2 is G or Q, X3 is I or V, X4 is L or A, X5 is DR or missing, X6 is N or T, X7 is P or T, X8 is D or E, X9 is S or T, X10 is F or Y, X11 is T or A, X12 is A or Y, X13 is Y or D, X14 is A or E, X15 is V or M, X16 is I or F, X17 is P or S, X18 is P or T, X19 is T or S, X20 is D or S, X21 is N or S, X22 is C or R, X23 is G or N, X24 is G or D, X25 is G or Q, X26 is V or D, X27 is Q or K, X28 is G or missing, X29 is R or K, X30 is C or S or V, X31 is A or G, X32 is G or A, X33 is S or G, X34 is G or S, X35 is G or Y, X36 is N or S or T or K, X37 is S or G, X38 is L or P, X39 is A or M, X40 is M or V and X41 is P or F.

On the basis of the process described above, two further production processes for the mistletoe lectin A-chain and mistletoe lectin B-chain or a fragment thereof are provided, which contain the following sequences or a fragment thereof:

Mistletoe Lectin A:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S

Mistletoe Lectin B:

D D V T C S A S E P T V R I V G R X21 G M X22 V D

V R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I W

X24 N G T I I N P R S N L V L A A S S G I K G T T

L T V Q T L D Y T L G Q G W L A G N D T A P R E

V T I Y G F R D L C M E S N X25 G S V W V E T C

X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R P K Q N

Q D Q C L T X30 G R D S V S T V I N I V S C S X31

X32 S X33 X34 Q R W V F T N E X35 A I L N L K X36 X37

X38 X39 X40 D V A Q A N P K L R R I I I Y P A T G

K P N Q M W L P V X41

A process according to the invention for the provision of a nucleic acid molecule, which codes for the above-mentioned mistletoe lectin polypeptide in a mistletoe cell or a transgenic mistletoe plant, comprises the following steps:

a) preparing of mistletoe cell RNA or chromosomal mistletoe cell DNA and

b) amplifying mistletoe cell RNA or chromosomal mistletoe lectin DNA by PCR using oligonucleotides which are derived from the mistletoe lectin polypeptide shown in Fig. 1b, and

c) if necessary, identifying of sequences which lie 5' and 3' from the amplified nucleic acid and amplification thereof, and

d) isolating of the nucleic acid molecules amplified in step b) and/or c), and

e) if necessary, ligating of several of the nucleic acid molecules isolated in step b) and/or c), such that a nucleic acid molecule with a complete open reading frame is obtained and

f) if necessary, targeted mutation of the nucleic acid molecule obtained in order to match the nucleic acid molecule to the usual genetic code for one of the mistletoe lectin polypeptide isoforms identified in mistletoe cells and/or to optimise expression.

Firstly, plant RNA or DNA is isolated preferably from fresh material by various generally known processes (Quiagen experimental protocol, Nickrent D L et al., American Journal of

Botany, vol.81, No.9 (1994): 1149-1160; Example 1). Using the degenerate oligonucleotides BI and BII described in Example 1, which are derived from the mistletoe lectin polypeptide shown in Figure 1b, the mistletoe lectin-I gene is amplified in a PCR reaction, the conditions for which are set out in Example 2. If this amplification step does not include the complete open reading frame of ML-I, the 5' and 3' region of the amplified nucleic acids can be identified using the RACE technique with the respective oligonucleotides stated in Example 3. The nucleic acid molecules thus obtained are isolated and if necessary ligated into a vector using suitable restriction cleavage sites in such a way that this contains the complete open reading frame. A nucleic acid molecule or a fragment thereof contained in this vector, which codes for a polypeptide such as described above in a mistletoe cell or a transgenic mistletoe plant, comprises the following sequence:

1) ML-I Sequence

TACGAGAGGCTAAGACTCAGAGTTACGCATCAAACCACGGGCGAKGAATACTTCCGGTTCATCACG

CTTCTCCGAGATTATGTCTCAAGCGGAAGCTTTTCCAATGAGATACCACTCTTGCGTCAGTCTACG

ATCCCCGTCTCCGATGCGCAAAGATTTGTCTTGGTGGAGCTCACCAACCAGGGGSRRGACTCGRTY

ACGGCCGCCATCGACGTTACCAATSYKTACGTCGTGGCTTACCAAGCAGGCGACCAATCCTACTTT

TTGCGCGACGCACCACGCGGCGCGGAAACGCACCTCTTCACCGGCACCACCCGAZ1TCCTCTCTCC

CATTCAMYGGAAGCTACMCYGATCTGGAGCGATACGCCGGACATAGGGACCAGATCCCTCTCGGTA

TAGASCAACTCATTCAATCCGTCWCKGCGCTTCGTTWYCCGGGCGGCAGCACGCGTRCYCAAGCTC

GTTCGATTTTAATCCTCATTCAGATGATCTCCGAGGCCGCCAGATTCAATCCCATCTTATGGAGGK

MYCGCCAAKAYATTAACAGTGGGGMRTCATTTCTGCCAGACRTGTACATGCTGGAGCTGGAGACGA

GTTGGGGCCAACAATCCACGCAAGTCCAGCATTCAACCGATGGCGTTTTTAATAACCCAWTYCGGT

TGGCTATAYCYMCYGGTAACTTCGTGACGTTGWCYAATGTTCGCKMYGTGATCGCCAGCTTGGCGA

TCATGTTGTTTGTATGCGGAGAGCGGCCATCTTCCTCTGACGTGCGCTATTGGCCGCTGGTCATAC

GACCCGTGATAGCCGATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAA

RTGGCATGYGCGTGGACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCT

CCAAGTCCAACAATGATCCGAATCAGTTGTGGACGATCAAAAGGGATRRMACCATTCGATCCAATG

GCAGCTGCTTGACCACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTG

CTGTGCGGGAGGCCACTATTTGGCAGATATGGGRCAATGGGACCATCATCAATCCAAGATCCAATC

TGGTTTTGGCAGCATCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTACACGT

TGGGACAGGGCTGGCTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGTTTCAGGG

ACCTTTGCATGGAATCAAATSRAGGGAGTGTGTGGGTGGAGACGTGCGWSAGTAGCCAAMAGAACC

AAZ2ARATGGGCTTTGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAAGACCAATGCCTCAC

CKBTGGGAGAGACTCCGTTTCAACAGTAATCAATATAGTTAGCTGCAGCGSWGSWTCGKSKKSKCA

GCGATGGGTGTTTACCAATGAAKRSGCCATTTTGAATTTAAAGAVWRGSYYGRYSRTGGATGTGGC

GCAAGCAAATCCAAAGCTCCGCCGAATAATTATCTATCCTGCCACAGGAAAACCAAATCAAATGTG

GCTTCCCGTGYYMTGA

A nucleic acid molecule according to the invention or a fragment thereof, which codes for one of the above-mentioned MLA polypeptides in a mistletoe cell or a transgenic mistletoe plant, comprises the following sequence:

II) MLA Sequence

TACGAGAGGCTAAGACTCAGAGTTACGCATCAAACCACGGGCGAKGAATACTTCCGGTTCATCACG

CTTCTCCGAGATTATGTCTCAAGCGGAAGCTTTTCCAATGAGATACCACTCTTGCGTCAGTCTACG

ATCCCCGTCTCCGATGCGCAAAGATTTGTCTTGGTGGAGCTCACCAACCAGGGGSRRGACTCGRTY

ACGGCCGCCATCGACGTTACCAATSYKTACGTCGTGGCTTACCAAGCAGGCGACCAATCCTACTTT

TTGCGCGACGCACCACGCGGCGCGGAAACGCACCTCTTCACCGGCACCACCCGAZ1TCCTCTCTCC

CATTCAMYGGAAGCTACMCYGATCTGGAGCGATACGCCGGACATAGGGACCAGATCCCTCTCGGTA

TAGASCAACTCATTCAATCCGTCWCKGCGCTTCGTTWYCCGGGCGGCAGCACGCGTRCYCAAGCTC

GTTCGATTTTAATCCTCATTCAGATGATCTCCGAGGCCGCCAGATTCAATCCCATCTTATGGAGGK

MYCGCCAAKAYATTAACAGTGGGGMRTCATTTCTGCCAGACRTGTACATGCTGGAGCTGGAGACGA

GTTGGGGCCAACAATCCACGCAAGTCCAGCATTCAACCGATGGCGTTTTTAATAACCCAWTYCGGT

TGGCTATAYCYMCYGGTAACTTCGTGACGTTGWCYAATGTTCGCKMYGTGATCGCCAGCTTGGCGA

Furthermore, a nucleic acid molecule or a fragment thereof, which codes for one of the above-mentioned MLB polypeptides in a mistletoe cell or a transgenic mistletoe plant, having the following sequence is made available:

III) MLB Sequence

GATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAARTGGCATGYGCGTG

GACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCTCCAAGTCCAACAAT

GATCCGAATCAGTTGTGGACGATCAAAAGGGATRRMACCATTCGATCCAATGGCAGCTGCTTGACC

ACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTGCTGTGCGGGAGGCC

ACTATTTGGCAGATATGGGRCAATGGGACCATCATCAATCCAAGATCCAATCTGGTTTTGGCAGCA

TCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTACACGTTGGGACAGGGCTGG

CTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGTTTCAGGGACCTTTGCATGGAA

TCAAATSRAGGGAGTGTGTGGGTGGAGACGTGCGWSAGTAGCCAAMAGAACCAAZ2ARATGGGCTT

TGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAAGACCAATGCCTCACCKBTGGGAGAGACT

CCGTTTCAACAGTAATCAATATAGTTAGCTGCAGCGSWGSWTCGKSKKSKCAGCGATGGGTGTTTA

CCAATGAAKRSGCCATTTTGAATTTAAAGAVWRGSYYGRYSRTGGATGTGGCGCAAGCAAATCCAA

AGCTCCGCCGAATAATTATCTATCCTGCCACAGGAAAACCAAATCAAATGTGGCTTCCCGTGYYMT

GA

The nucleotides are defined in accordance with the IUPAC-IUB code; in addition, Z_1 designates the nucleotide sequence GAT AGA or is missing, while Z_2 designates the nucleotide GGC or is missing.

A specific nucleic acid molecule which is to be expressed in a mistletoe cell or in a transgenic mistletoe plant and codes for ML-I, is shown in Figure 1a. Furthermore, specific nucleic acid

plants, which are modified in their codon usage in such a manner that as a result the expression rate is optimised.

Furthermore, the present invention makes available a process for the production of one of the above-described polypeptides, which includes the modification of sugar side-chains by enzymatic and/or chemical addition, removal and/or modification of one or several side-chains (Macindoe W M et al., Carbohydrate Research, 1995, **269** (2): 227-57; Meynial-Salles I and Combes D, J. Biotechnol., 1996, **46** (1), 1-14; Wong S Y, Current Opinion in Structural Biology, 1995, **5** (5), 599-604). In this way, the in vivo activity of individual MLA and/or MLB chains can be strengthened or weakened or in the event of any variations dependent on the expression system can be optimally matched to the natural mistletoe lectins. It is also intended that such modified mistletoe lectin can be added to a pharmaceutical composition according to the invention.

The following figures and examples illustrate the invention:

Fig.A: Representation of a mistletoe lectin-I dimer.

Fig.1: Representation of the (a) nucleic acid sequence and (b) amino acid sequence of ML-I.

Fig.2: Representation of the (a) nucleic acid sequence and (b) amino acid sequence of mistletoe lectin A1.

Fig.3: Representation of the (a) nucleic acid sequence and (b) amino acid sequence of mistletoe lectin A2.

Fig.4: Representation of the nucleic acid sequence of MLI, wherein the nucleic acid sequence is matched to the codon usage of *Brassica*.

Fig.5: Representation of the nucleic acid sequence of mistletoe lectin A1, wherein the nucleic acid sequence is matched to the codon usage of *Brassica*.

Fig.6: Representation of the nucleic acid sequence of mistletoe lectin A2, wherein the nucleic acid sequence is matched to the codon usage of *Brassica*.

Fig.7: Representation of the (a) nucleic acid sequence and (b) amino acid sequence of mistletoe lectin B.

Fig.8: Representation of the (a) nucleic acid sequence and (b) amino acid sequence of mistletoe lectin B1.

Fig.9: Representation of the (a) nucleic acid sequence and (b) amino acid sequence of

mistletoe lectin B2.

Fig. 10: Representation of the (a) nucleic acid sequence and (b) amino acid sequence of mistletoe lectin B3.

Fig. 11: Representation of the (a) nucleic acid sequence and (b) amino acid sequence of mistletoe lectin B4.

Fig. 12: Representation of the (a) nucleic acid sequence and (b) amino acid sequence of mistletoe lectin B5.

Fig. 13: Representation of the nucleic acid sequence of mistletoe lectin B, wherein the nucleic acid sequence is matched to the codon usage of *Brassica*.

Fig. 14: Representation of the nucleic acid sequence of mistletoe lectin B1, wherein the nucleic acid sequence is matched to the codon usage of *Brassica*.

Fig. 15: Representation of the nucleic acid sequence of mistletoe lectin B2, wherein the nucleic acid sequence is matched to the codon usage of *Brassica*.

Fig. 16: Representation of the nucleic acid sequence of mistletoe lectin B3, wherein the nucleic acid sequence is matched to the codon usage of *Brassica*.

Fig. 17: Representation of the nucleic acid sequence of mistletoe lectin B4, wherein the nucleic acid sequence is matched to the codon usage of *Brassica*.

Fig. 18: Representation of the nucleic acid sequence of mistletoe lectin B5, wherein the nucleic acid sequence is matched to the codon usage of *Brassica*.

Example 1

Mistletoe plants of the species *Viscum album L. spp. platyspermum* Kell were harvested from poplars growing in Alsace and frozen directly after harvesting. The plant material was crushed in liquid nitrogen in the laboratory and then the DNA from 100 mg of plant material was isolated by the process described in the Qiagen DNeasy Plant Mini-Handbook 09/96.

Example 2

PCR Conditions for the Amplification of Mistletoe Lectin-I DNA

For the amplification of genomic mistletoe lectin-I DNA, 100 ng of template DNA, prepared as stated in Example 1, were used in a PCR process with 30 cycles using Taq polymerase (Boehringer Mannheim). 1 μg of primer, $MgCl_2$ (end concentration 2 mM), nucleotide mixture A, T, C, G (end concentration 0.2 mM) and 2.5 units of Taq polymerase were added

to the template DNA. The reaction was started as hot-start PCR by a denaturation step of the DNA for 5 minutes at 94°C. In this, the enzyme and the remaining reagents only mixed after a wax barrier between the components had melted. The 30 subsequent cycles are performed under the following conditions:

Denaturation:	94°C	30 seconds
Annealing:	55°C	30 seconds
Amplification:	72°C	1 minute.

Following the 30 cycles, a 7-minute elongation reaction at 72°C was also performed, before the reaction mixture was cooled down to 4°C.

The primers used in the PCR process hybridised with fragments of the genomic DNA coding for MLB chain DNA and had the following sequences:

B1. GTN MGN GAY GAY GAY TTY CA

B2. AT YTG RTT NGG YTT NCC NGT

The nucleotides are defined in accordance with the IUPAC-IUB code.

The oligonucleotide B1 hybridised to the nucleic acid region that corresponds to amino acids 24 to 30 of the MLB sequence, while the oligonucleotide B2 hybridised to the complementary DNA sequence coding for amino acids 253-258 of MLB.

Example 3

In order to determine the flanking 3' and 5' sequences of the DNA amplified in Example 2, the RACE technique was used. 2 μg of RNA template in cDNA synthesis buffer (end concentration: 20 mM Tris-HCl, 8 mM $MgCl_2$, 30 mM KCl, 1 mM dithiothreitol; pH 8.5 (20°C)) were treated with AMV reverse transcriptase, the deoxynucleotides and the specific primer (see below) and incubated for 60 mins at 65°C. Next, the sample was incubated for 10 mins at 65°C. After the purification of the first cDNA strand, the "tailing" reaction was carried out with 2/5 of the synthesised cDNA with terminal transferase. After the tailing reaction, a PCR was performed with the oligo-dT anchor primer and the specific primer (see above for incubation conditions, except for the annealing temperature, which was lowered to

50°C). For the determination of the 5' regions of the nucleic acid molecules amplified in Example 2, the oligonucleotide having the following sequence was used:
CAC AGC AGT ATT ACA GTC GAA.

A DNA sequence complementary to this oligonucleotide codes for the amino acid sequence 79-85 of the MLB polypeptide. In order to determine the 3' regions of the amplified nucleic acid molecules, the oligonucleotide having the following sequence was used in a similar experiment:
GTC TAT GTG ATG ATC TTC GAC TGT.

This nucleic acid sequence codes for the amino acid region 74-81 of the MLB polypeptide. For the 3' RACE reaction, the same incubation conditions as for the 5' RACE were used, except for the "tailing" reaction, which is not necessary here because of the polyA tail of the mRNA. In both processes, the oligo-dT anchor primer of the Boehringer Mannheim kit was used.

Example 4

Pharmaceutical Composition with Cytotoxic Action:

Mistletoe, tobacco and rape cells are transfected with RNA vectors which code for MLA1 and MLA2, the respective cells are harvested after a few days, and the MLA1 and MLA2 proteins purified by affinity chromatography. As gel material, divinylsulphone (DVS)-activated lactose-coupled Sepharose 4B (Pharmacia) is used. By treatment with 0.2 M HCl, the material is activated, i.e. the Sepharose structure is partially hydrolysed and sugar-binding sites to which the lectins can bind are freed. 100 ml of gel material are washed with 0.2 M HCl in a Buchner funnel and suspended in 200 ml of 0.2 M HCl. The hydrolysis of the gel material is effected by 3.5-hour incubation of the suspension at 50°C in the water-bath. The suspension is washed free of acid with water and then with peptide eluent (0.05 K_2HPO_4x $3H_2O$, 0.15 M NaCl, pH 7.0). Then the suspension is degassed, the peptide eluent removed by suction, and the viscous liquid gel material filled into an empty column XK50/30 (3 x 50 cm, Pharmacia) and packed with peptide eluent pH 7.0 at a flow rate of 2.5 ml/min initially and then 5 ml/min. The column is equilibrated with the same eluent at a flow rate of 1 ml/min. The cell extract obtained from the transfected mistletoe cells is centrifuged and the supernatant loaded onto the column. The separation is performed at a flow rate of 1 ml/min with peptide

eluent pH 7.0. The lectins are eluted from the column material with a buffer of 0.2 M lactose in peptide eluent pH 7.0 at a flow rate of 2 ml/min. The elution of the lectin from the column is measured by determination of the absorption at 206 nm. The lectin-containing fractions are collected, frozen and lyophilised. If desired, a further purification step on an HPLC column can be performed. Suitable for this is a Vydac C4 300 A column, which is run at a flow rate of 300 µl/min and a gradient of 20% to 100% B in 60 minutes, where eluent A is 0.17% TFA in water and eluent B is 0.15% TFA in 80% CH_3CN in water. The elution of the mistletoe lectins is detected at a wavelength of 214 nm.

The purified MLA-1 and MLA-2 polypeptides are coupled to a suitable cell recognition molecule. If the cell recognition molecule is a mono- or polyclonal antibody, this can for example be bound to the cytotoxic MLA1 or MLA2 using glutaraldehyde or be directly expressed as chimaeric fusion protein (antibody-MLA) in the appropriate expression system.

Example 5

Pharmaceutical Composition:

Mistletoe cells are transfected with RNA vectors which code for the mistletoe lectins MLA1 and MLA2 and mistletoe lectins MLB to MLB6. After a few days, the mistletoe lectin monomers or dimers are extracted from the mistletoe cells and purified by processes such as are described in Example 4. The monomers thus obtained can be fused in vitro to heterologous and homologous dimers. In this way, a large number of different combinations of the individual MLA and MLB polypeptides are formed. The heterogeneous mixture of ML-1 dimers and monomers thus produced is lyophilised and used for formulation with a suitable vehicle.

Patent Claims

1. Process for the production of a mistletoe lectin polypeptide in the heterologous system having the sequence:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S D V R Y W P L V I R P V I A D D

V T C S A S E P T V R I V G R X21 G M X22 V D V

R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I

W X24 N G T I I N P R S N L V L A A S S G I K G

T T L T V Q T L D Y T L G Q G W L A G N D T A

P R E V T I Y G F R D L C M E S N X25 G S V W V

E T C X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R

P K Q N Q D Q C L T X30 G R D S V S T V I N I V

S C S X31 X32 S X33 X34 Q R W V F T N E X35 A I L N

L K X36 X37 X38 X39 X40 D V A Q A N P K L R R I I I

Y P A T G K P N Q M W L P V X41

or a fragment thereof, comprising the step of expressing by means of a eukaryotic or prokaryotic vector, into which a nucleic acid coding for the mistletoe lectin polypeptide according to the usual genetic code or a fragment thereof is cloned, in a suitable heterologous eukaryotic or prokaryotic host,

wherein X1 is D or E, X2 is G or Q, X3 is I or V, X4 is L or A, X5 is DR or missing, X6 is N or T, X7 is P or T, X8 is D or E, X9 is S or T, X10 is F or Y, X11 is T or A, X12 is A or Y, X13 is Y or D, X14 is A or E, X15 is V or M, X16 is I or F, X17 is P or S, X18 is P or T, X19 is T or S, X20 is D or S, X21 is N or S, X22 is C or R, X23 is G or N, X24 is G or D, X25 is G or Q, X26 is V or D, X27 is Q or K, X28 is G or missing, X29 is R or K, X30 is C or S or V, X31 is A or G, X32 is G or A, X33 is S or G, X34 is G or S, X35 is G or Y, X36 is N or S or T or K, X37 is S or G, X38 is L or P, X39 is A or M, X40 is M or V and X41 is P or F.

2. Process according to Claim 1, wherein the mistletoe lectin polypeptide corresponds to the mistletoe lectin A-chain (MLA) or a fragment thereof, and contains the following sequence or a fragment thereof:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S

wherein X1 to X20 have the meaning stated above.

3. Process according to Claim 1, wherein the mistletoe lectin polypeptide corresponds to the mistletoe lectin B-chain (MLB) or a fragment thereof, and contains the following sequence or a fragment thereof:

D D V T C S A S E P T V R I V G R X21 G M X22 V D

V R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I W

X24 N G T I I N P R S N L V L A A S S G I K G T T

L T V Q T L D Y T L G Q G W L A G N D T A P R E

V T I Y G F R D L C M E S N X25 G S V W V E T C

X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R P K Q N

Q D Q C L T X30 G R D S V S T V I N I V S C S X31

X32 S X33 X34 Q R W V F T N E X35 A I L N L K X36 X37

X38 X39 X40 D V A Q A N P K L R R I I I Y P A T G

K P N Q M W L P V X41

wherein X21 to X41 have the meaning stated above.

4. Mistletoe lectin polypeptide having the following sequence:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S D V R Y W P L V I R P V I A D D

V T C S A S E P T V R I V G R X21 G M X22 V D V

R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I

W X24 N G T I I N P R S N L V L A A S S G I K G

T T L T V Q T L D Y T L G Q G W L A G N D T A

P R E V T I Y G F R D L C M E S N X25 G S V W V

E T C X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R

P K Q N Q D Q C L T X30 G R D S V S T V I N I V

S C S X31 X32 S X33 X34 Q R W V F T N E X35 A I L N

L K X36 X37 X38 X39 X40 D V A Q A N P K L R R I I I

Y P A T G K P N Q M W L P V X41

or a fragment thereof,

wherein X1 is D or E, X2 is G or Q, X3 is I or V, X4 is L or A, X5 is DR or missing, X6 is N or T, X7 is P or T, X8 is D or E, X9 is S or T, X10 is F or Y, X11 is T or A, X12 is A or Y, X13 is Y or D, X14 is A or E, X15 is V or M, X16 is I or F, X17 is P or S, X18 is P or T, X19 is T or S, X20 is D or S, X21 is N or S, X22 is C or R, X23 is G or N, X24 is G or D, X25 is G or Q, X26 is V or D, X27 is Q or K, X28 is G or missing, X29 is R or K, X30 is C or S or V, X31 is A or G, X32 is G or A, X33 is S or G, X34 is G or S, X35 is G or Y, X36 is N or S or T or K, X37 is S or G, X38 is L or P, X39 is A or M, X40 is M or V and X41 is P or F.

5. Mistletoe lectin polypeptide according to Claim 4, comprising the sequence:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S

or a fragment of this sequence, wherein the mistletoe lectin polypeptide corresponds to the MLA chain or a fragment thereof and X1 to X20 have the meaning stated above.

6. Mistletoe lectin polypeptide according to Claim 4, comprising the sequence:

D D V T C S A S E P T V R I V G R X21 G M X22 V D

V R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I W

X24 N G T I I N P R S N L V L A A S S G I K G T T

L T V Q T L D Y T L G Q G W L A G N D T A P R E

V T I Y G F R D L C M E S N X25 G S V W V E T C

X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R P K Q N

Q D Q C L T X30 G R D S V S T V I N I V S C S X31

X32 S X33 X34 Q R W V F T N E X35 A I L N L K X36 X37

X38 X39 X40 D V A Q A N P K L R R I I I Y P A T G

K P N Q M W L P V X41

or a fragment of this sequence, wherein the mistletoe lectin polypeptide corresponds to the MLB chain or a fragment thereof and X21 to X41 have the meaning stated above.

7. Mistletoe lectin polypeptide according Claim 4, having the sequence shown in Fig. 1b.

8. Mistletoe lectin polypeptide according Claim 5, having the sequence shown in Fig. 3b.

9. Mistletoe lectin polypeptide according to Claim 6, selected from the following group:

I) Polypeptide having the sequence shown in Fig. 7b.
II) Polypeptide having the sequence shown in Fig. 8b.
III) Polypeptide having the sequence shown in Fig. 9b.
IV) Polypeptide having the sequence shown in Fig. 10b.
V) Polypeptide having the sequence shown in Fig. 11b.
VI) Polypeptide having the sequence shown in Fig. 12b.

10. Process for the preparation of a nucleic acid molecule which codes for a mistletoe lectin polypeptide according to Claim 4 in a heterologous host, comprising the steps:

a) preparing of mistletoe cell RNA or chromosomal mistletoe cell DNA and

b) amplifying mistletoe cell RNA or chromosomal mistletoe lectin DNA by PCR using oligonucleotides which are derived from the mistletoe lectin polypeptide shown in Fig. 1b, and

c) if necessary, identifying of sequences which lie 5' and 3' from the amplified nucleic acid and amplification thereof, and

d) isolating of the nucleic acid molecules amplified in step b) and/or c), and

e) if necessary, ligating several of the nucleic acid molecules amplified in step b) and/or c), such that a nucleic acid molecule with a complete open reading frame is obtained and

f) targeted mutation of the nucleic acid molecule obtained in order to match the nucleic acid molecule to the usual genetic code of the heterologous host for one of the mistletoe lectin polypeptide isoforms identified in mistletoe cells.

11. Nucleic acid molecule, coding for a polypeptide according to Claim 4 and comprising the sequence:

TACGAGAGGCTAAGACTCAGAGTTACGCATCAAACCACGGGCGAKGAATACTTCCGGTTCATCACG

CTTCTCCGAGATTATGTCTCAAGCGGAAGCTTTTCCAATGAGATACCACTCTTGCGTCAGTCTACG

ATCCCCGTCTCCGATGCGCAAAGATTTGTCTTGGTGGAGCTCACCAACCAGGGGSRRGACTCGRTY

ACGGCCGCCATCGACGTTACCAATSYKTACGTCGTGGCTTACCAAGCAGGCGACCAATCCTACTTT

TTGCGCGACGCACCACGCGGCGCGGAAACGCACCTCTTCACCGGCACCACCCGAZ1TCCTCTCTCC

CATTCAMYGGAAGCTACMCYGATCTGGAGCGATACGCCGGACATAGGGACCAGATCCCTCTCGGTA

TAGASCAACTCATTCAATCCGTCWCKGCGCTTCGTTWYCCGGGCGGCAGCACGCGTRCYCAAGCTC

GTTCGATTTTAATCCTCATTCAGATGATCTCCGAGGCCGCCAGATTCAATCCCATCTTATGGAGGK

MYCGCCAAKAYATTAACAGTGGGGMRTCATTTCTGCCAGACRTGTACATGCTGGAGCTGGAGACGA

GTTGGGGCCAACAATCCACGCAAGTCCAGCATTCAACCGATGGCGTTTTTAATAACCCAWTYCGGT

TGGCTATAYCYMCYGGTAACTTCGTGACGTTGWCYAATGTTCGCKMYGTGATCGCCAGCTTGGCGA

TCATGTTGTTTGTATGCGGAGAGCGGCCATCTTCCTCTGACGTGCGCTATTGGCCGCTGGTCATAC

GACCCGTGATAGCCGATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAA

RTGGCATGYGCGTGGACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCT

CCAAGTCCAACAATGATCCGAATCAGTTGTGGACGATCAAAAGGGATRRMACCATTCGATCCAATG

GCAGCTGCTTGACCACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTG

CTGTGCGGGAGGCCACTATTTGGCAGATATGGGRCAATGGGACCATCATCAATCCAAGATCCAATC

TGGTTTTGGCAGCATCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTACACGT

TGGGACAGGGCTGGCTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGTTTCAGGG

ACCTTTGCATGGAATCAAATSRAGGGAGTGTGTGGGTGGAGACGTGCGWSAGTAGCCAAMAGAACC

AAZ2ARATGGGCTTTGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAAGACCAATGCCTCAC

CKBTGGGAGAGACTCCGTTTCAACAGTAATCAATATAGTTAGCTGCAGCGSWGSWTCGKSKKSKCA

GCGATGGGTGTTTACCAATGAAKRSGCCATTTTGAATTTAAAGAVWRGSYYGRYSRTGGATGTGGC

GCAAGCAAATCCAAAGCTCCGCCGAATAATTATCTATCCTGCCACAGGAAAACCAAATCAAATGTG

GCTTCCCGTGYYMTGA

or a fragment thereof, wherein the nucleotides are defined in accordance with the IUPAC-IUB code, and Z_1 designates the nucleotide sequence GAT AGA or is missing and Z_2 designates the nucleotide sequence GGC or is missing.

12. Nucleic acid molecule which codes for a polypeptide according to Claim 5 in a heterologous host, comprising the sequence:

TACGAGAGGCTAAGACTCAGAGTTACGCATCAAACCACGGGCGAKGAATACTTCCGGTTCATCACG

CTTCTCCGAGATTATGTCTCAAGCGGAAGCTTTTCCAATGAGATACCACTCTTGCGTCAGTCTACG

ATCCCCGTCTCCGATGCGCAAAGATTTGTCTTGGTGGAGCTCACCAACCAGGGGSRRGACTCGRTY

ACGGCCGCCATCGACGTTACCAATSYKTACGTCGTGGCTTACCAAGCAGGCGACCAATCCTACTTT

TTGCGCGACGCACCACGCGGCGCGGAAACGCACCTCTTCACCGGCACCACCCGAZ1TCCTCTCTCC

CATTCAMYGGAAGCTACMCYGATCTGGAGCGATACGCCGGACATAGGGACCAGATCCCTCTCGGTA

TAGASCAACTCATTCAATCCGTCWCKGCGCTTCGTTWYCCGGGCGGCAGCACGCGTRCYCAAGCTC

GTTCGATTTTAATCCTCATTCAGATGATCTCCGAGGCCGCCAGATTCAATCCCATCTTATGGAGGK

MYCGCCAAKAYATTAACAGTGGGGMRTCATTTCTGCCAGACRTGTACATGCTGGAGCTGGAGACGA

GTTGGGGCCAACAATCCACGCAAGTCCAGCATTCAACCGATGGCGTTTTTAATAACCCAWTYCGGT

TGGCTATAYCYMCYGGTAACTTCGTGACGTTGWCYAATGTTCGCKMYGTGATCGCCAGCTTGGCGA

TCATGTTGTTTGTATGCGGAGAGCGGCCATCTTCCTCT

or a fragment thereof, wherein the nucleotides are defined in accordance with the IUPAC-IUB code, and Z_1 designates the nucleotide sequence GAT AGA or is missing.

13. Nucleic acid which codes for a polypeptide according to Claim 6 in a heterologous host, comprising the sequence:

GATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAARTGGCATGYGCGTG

GACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCTCCAAGTCCAACAAT

GATCCGAATCAGTTGTGGACGATCAAAAGGGATRRMACCATTCGATCCAATGGCAGCTGCTTGACC

ACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTGCTGTGCGGGAGGCC

ACTATTTGGCAGATATGGGRCAATGGGACCATCATCAATCCAAGATCCAATCTGGTTTTGGCAGCA

TCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTACACGTTGGGACAGGGCTGG

CTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGTTTCAGGGACCTTTGCATGGAA

TCAAATSRAGGGAGTGTGTGGGTGGAGACGTGCGWSAGTAGCCAAMAGAACCAAZ2ARATGGGCTT

TGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAAGACCAATGCCTCACCKBTGGGAGAGACT

CCGTTTCAACAGTAATCAATATAGTTAGCTGCAGCGSWGSWTCGKSKKSKCAGCGATGGGTGTTTA

CCAATGAAKRSGCCATTTTGAATTTAAAGAVWRGSYYGRYSRTGGATGTGGCGCAAGCAAATCCAA

AGCTCCGCCGAATAATCATCTATCCTGCCACAGGAAAACCAAATCAAATGTGGCTTCCCGTGYYMT

GA

or a fragment thereof, wherein the nucleotides are defined in accordance with the IUPAC-IUB code, and Z_2 designates the nucleotide sequence GGC or is missing.

14. Nucleic acid molecule according to Claim 11, having the sequence shown in Fig. 1a.

15. Nucleic acid molecule according to Claim 12, selected from the following group:

I) Nucleic acid having the sequence shown in Fig. 2a.

II) Nucleic acid having the sequence shown in Fig. 3a.

or a fragment thereof.

16. Nucleic acid molecule according to Claim 13, selected from the following group:

I) Nucleic acid with the sequence shown in Fig. 7a.

II) Nucleic acid with the sequence shown in Fig.8a.

III) Nucleic acid with the sequence shown in Fig.9a.

IV) Nucleic acid with the sequence shown in Fig.10a.

V) Nucleic acid with the sequence shown in Fig.11a.

VI) Nucleic acid with the sequence shown in Fig.12a.

or a fragment thereof.

17. Nucleic acid molecule coding for a mistletoe lectin polypeptide according to at least one of Claims 4 to 9 or for a fragment thereof, wherein the codon usage is adapted to the requirements of a heterologous host.

18. Nucleic acid molecule according to Claim 17 having the sequence shown in Fig.4a, wherein the codon usage is adapted to the preferred codon usage of the genus Brassica.

19. Nucleic acid molecule according to Claim 17, selected from the following group:

I) Nucleic acid with the sequence shown in Fig.5a,

II) Nucleic acid with the sequence shown in Fig.6a.

20. Nucleic acid molecule according to Claim 17, selected from the following group:

I) Nucleic acid with the sequence shown in Fig.13a,

II) Nucleic acid with the sequence shown in Fig.14a,

III) Nucleic acid with the sequence shown in Fig.15a,

IV) Nucleic acid with the sequence shown in Fig.16a,

V) Nucleic acid with the sequence shown in Fig.17a,

VI) Nucleic acid with the sequence shown in Fig.18a.

21. Vector which comprises a nucleic acid molecule according to one of Claims 11 to 20 or a fragment thereof and a promoter functionally linked thereto.

22. Vector according to Claim 21, wherein the promoter is a specific promoter for an intended host cell.

23. Vector according to Claim 21 and/or 22, wherein the vector is an RNA vector.

24. Host cell for carrying out the process according to one of Claims 1 to 3, which can be a bacterial cell, a plant cell with the exception of a mistletoe cell, an insect larva, an insect cell, a vertebrate cell, preferably a mammalian cell, a yeast cell, a fungal cell, a transgenic vertebrate and/or a transgenic plant with the exception of a mistletoe plant and contains a nucleic acid molecule according to one of Claims 11 to 20 or a vector according to one of Claims 21 to 23.

25. Host cell according to Claim 24, wherein the bacterial cell is Escherichia coli and/or the plant cell is a rape cell and/or the insect larva cell is Trichoplusia ni and/or the insect cell is a Spodoptera frugiperda cell and/or the vertebrate is a zebra fish.

26. Pharmaceutical composition, containing at least one nucleic acid molecule according to one of Claims 11 to 20 or at least one vector according to one of Claims 21 to 23.

27. Pharmaceutical composition according to Claim 26, further containing liposomes.

28. Pharmaceutical composition according to Claim 27, wherein the liposomes bear cell recognition molecules on their surface, wherein the cell recognition molecule selectively binds to target cells.

29. Pharmaceutical composition according to Claim 26, further containing MLB polypeptide according to one of Claims 6 or 9.

30. Pharmaceutical composition according to Claim 29, wherein the MLB polypeptide or the nucleic acid molecule or the vector is coupled to a cell recognition molecule, wherein the cell recognition molecule selectively binds to target cells.

31. Pharmaceutical composition according to Claim 26, wherein the nucleic acid or the vector are associated with a virus particle.

32. Pharmaceutical composition according to Claim 31, wherein the virus particle bears a cell recognition molecule on its surface, wherein the cell recognition molecule selectively binds to target cells.

33. Pharmaceutical composition which contains at least one polypeptide according to Claim 4 to 9 and/or a fragment thereof.

34. Pharmaceutical composition according to Claim 33, further containing a suitable cell recognition molecule, wherein the cell recognition molecule selectively binds to target cells.

35. Pharmaceutical composition according to Claim 34, wherein the cell recognition molecule is selected from the group comprising antibody molecules or antibody fragments, cell receptor ligands, peptide hormones or fragments thereof.

36. Use of a mistletoe lectin polypeptide according to at least one of Claims 4 to 9 and/or a fragment thereof for the production of a medicament for the treatment of uncontrolled cell growth.

37. Use of a mistletoe lectin polypeptide according to at least one of Claims 4 to 9 and/or a fragment thereof without cytotoxic activity for the production of a medicament which intensifies the immune reaction.

38. Use according to Claim 37, wherein the medicament includes a further antigen.

39. Use according to Claim 38, wherein the further antigen is a tumour-induced antigen, a bacterial or viral antigen.

40. Process for the production of a mistletoe lectin polypeptide in mistletoe cells and/or a transgenic mistletoe plant having the sequence:

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S D V R Y W P L V I R P V I A D D

V T C S A S E P T V R I V G R X21 G M X22 V D V

R D D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D X23 T I R S N G S C L T T Y G Y

T A G V Y V M I F D C N T A V R E A T I W Q I

W X24 N G T I I N P R S N L V L A A S S G I K G

T T L T V Q T L D Y T L G Q G W L A G N D T A

P R E V T I Y G F R D L C M E S N X25 G S V W V

E T C X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R

P K Q N Q D Q C L T X30 G R D S V S T V I N I V

S C S X31 X32 S X33 X34 Q R W V F T N E X35 A I L N

L K X36 X37 X38 X39 X40 D V A Q A N P K L R R I I I

Y P A T G K P N Q M W L P V X41

or a fragment thereof, comprising the step of expressing by means of a eukaryotic vector, which contains a nucleic acid coding for the mistletoe lectin polypeptide or a fragment thereof having the nucleic acid sequence originally found in mistletoe cell DNA, in a mistletoe cell and/or a transgenic mistletoe plant, wherein the transcription product of this nucleic acid molecule is modified in mistletoe cells and/or transgenic mistletoe plants by postranscriptional and/or posttranslational mechanisms, wherein X1 is D or E, X2 is G or Q, X3 is I or V, X4 is L or A, X5 is DR or missing, X6 is N or T, X7 is P or T, X8 is D or E, X9 is S or T, X10 is F or Y, X11 is T or A, X12 is A or Y, X13 is Y or D, X14 is A or E, X15 is V or M, X16 is I or F, X17 is P or S, X18 is P or T, X19 is T or S, X20 is D or S, X21 is N or S, X22 is C or R, X23 is G or N, X24 is G or D, X25 is G or Q, X26 is V or D, X27 is Q or K, X28 is G or

missing, X29 is R or K, X30 is C or S or V, X31 is A or G, X32 is G or A, X33 is S or G, X34 is G or S, X35 is G or Y, X36 is N or S or T or K, X37 is S or G, X38 is L or P, X39 is A or M, X40 is M or V and X41 is P or F.

41. Process according to Claim 40, wherein the mistletoe lectin polypeptide corresponds to the mistletoe lectin A-chain or a fragment thereof and includes the following sequence or a fragment thereof :

Y E R L R L R V T H Q T T G X1 E Y F R F I T L

L R D Y V S S G S F S N E I P L L R Q S T I P

V S D A Q R F V L V E L T N Q G X2 D S X3 T A A

I D V T N X4 Y V V A Y Q A G D Q S Y F L R D A

P R G A E T H L F T G T T R X5 S S L P F X6 G S

Y X7 D L E R Y A G H R D Q I P L G I X8 Q L I Q

S V X9 A L R X10 P G G S T R X11 Q A R S I L I L

I Q M I S E A A R F N P I L W R X12 R Q X13 I N

S G X14 S F L P D X15 Y M L E L E T S W G Q Q S

T Q V Q H S T D G V F N N P X16 R L A I X17 X18 G

N F V T L X19 N V R X20 V I A S L A I M L F V C

G E R P S S S

wherein X1 to X20 have the meaning stated above.

42. Process according to Claim 40, wherein the mistletoe lectin polypeptide corresponds to the mistletoe lectin B-chain or a fragment thereof and includes the following sequence or a fragment thereof :

D D V T C S A S E P T V R I V G R X21 G M X22 V D
V R D D D F H D G N Q I Q L W P S K S N N D P N
Q L W T I K R D X23 T I R S N G S C L T T Y G Y
T A G V Y V M I F D C N T A V R E A T I W Q I W
X24 N G T I I N P R S N L V L A A S S G I K G T T
L T V Q T L D Y T L G Q G W L A G N D T A P R E
V T I Y G F R D L C M E S N X25 G S V W V E T C
X26 S S Q X27 N Q X28 X29 W A L Y G D G S I R P K Q N
Q D Q C L T X30 G R D S V S T V I N I V S C S X31
X32 S X33 X34 Q R W V F T N E X35 A I L N L K X36 X37
X38 X39 X40 D V A Q A N P K L R R I I I Y P A T G
K P N Q M W L P V X41

wherein X21 to X41 have the meaning stated above.

43. Process for the preparation of a nucleic acid molecule, which codes for a mistletoe lectin polypeptide according to Claim 4 in a mistletoe cell and/or a transgenic mistletoe plant, comprising the steps:

a) preparing of mistletoe cell RNA or chromosomal mistletoe cell DNA and

b) amplifying mistletoe cell RNA or chromosomal mistletoe lectin DNA by PCR using oligonucleotides which are derived from the mistletoe lectin polypeptide shown in Fig. 1b, and

c) if necessary, identifying of sequences which lie 5' and 3' from the amplified nucleic acid and amplification thereof, and

d) isolating of the nucleic acid molecules amplified in step b) and/or c), and

e) if necessary, ligating several of the nucleic acid molecules isolated in step b) and/or c), such that a nucleic acid molecule with a complete open reading frame is obtained and

f) if necessary, targeted mutation of the nucleic acid molecule obtained in order to match the nucleic acid molecule to the usual genetic code for one of the mistletoe lectin polypeptide isoforms identified in mistletoe cells and/or to optimise expression.

44. Process for production of a polypeptide according to one of Claims 1 to 3 or 40 to 42, including as a further step the modification of sugar side-chains by enzymatic and/or chemical addition, removal and/or modification of one or several side-chains.

45. Process according to Claim 44, wherein the addition, removal and/or modification of the sugar side-chains leads to matching to the natural proteins.

Fig. A

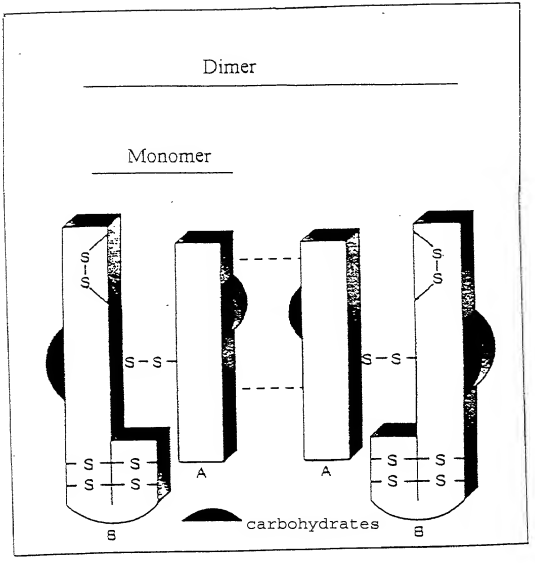

Fig. 1a

mistletoe lectin I

TACGAGAGGCTAAGACTCAGAGTTACGCATCAAACCACGGGGCGAGGAATACTTCCGGTTCATC

ACGCTTCTCCGAGATTATGTCTCAAGCGGAAGCTTTTCCAATGAGATACCACTCTTGCGTCAG

TCTACGATCCCCGTCTCCGATGCGCAAAGATTTGTCTTGGTGGAGCTCACCAACCAGGGGGGA

GACTCGATCACGGCCGCCATCGACGTTACCAATCTGTACGTCGTGGCTTACCAAGCAGGCGAC

CAATCCTACTTTTTGCGCGACGCACCACGCGGCGCGGAAACGCACCTCTTCACCGGCACCACC

CGATCCTCTCTCCCATTCAACGGAAGCTACCCTGATCTGGAGCGATACGCCGGACATAGGGAC

CAGATCCCTCTCGGTATAGACCAACTCATTCAATCCGTCACGGCGCTTCGTTTTCCGGGCGGC

AGCACGCGTACCCAAGCTCGTTCGATTTTAATCCTCATTCAGATGATCTCCGAGGCCGCCAGA

TTCAATCCCATCTTATGGAGGGCTCGCCAATACATTAACAGTGGGGCGTCATTTCTGCCAGAC

GTGTACATGCTGGAGCTGGAGACGAGTTGGGGCCAACAATCCACGCAAGTCCAGCATTCAACC

GATGGCGTTTTTAATAACCCAATTCGGTTGGCTATACCCCCCGGTAACTTCGTGACGTTGACC

AATGTTCGCGACGTGATCGCCAGCTTGGCGATCATGTTGTTTGTATGCGGAGAGCGGCCATCT

TCCTCTGACGTGCGCTATTGGCCGCTGGTCATACGACCCGTGATAGCCGATGATGTTACCTGC

AGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAAATGGCATGTGCGTGGACGTCCGAGAT

GACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCTCCAAGTCCAACAATGATCCGAAT

CAGTTGTGGACGATCAAAAGGGATGGAACCATTCGATCCAATGGCAGCTGCTTGACCACGTAT

GGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTGCTGTGCGGGAGGCCACT

ATTTGGCAGATATGGGGCAATGGGACCATCATCAATCCAAGATCCAATCTGGTTTTGGCAGCA

TCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTACACGTTGGGACAGGGC

TGGCTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGTTTCAGGGACCTTTGC

ATGGAATCAAATGGAGGGAGTGTGTGGGTGGAGACGTGCGTGAGTAGCCAACAGAACCAAAGA

TGGGCTTTGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAAGACCAATGCCTCACCTGT

GGGAGAGACTCCGTTTCAACAGTAATCAATATAGTTAGCTGCAGCGCTGGATCGTCTGGGCAG

CGATGGGTGTTTACCAATGAAGGGGCCATTTTGAATTTAAAGAATGGGTTGGCCATGGATGTG

GCGCAAGCAAATCCAAAGCTCCGCCGAATAATTATCTATCCTGCCACAGGAAAACCAAATCAA

ATGTGGCTTCCCGTGCCATGA

Fig. 1b

mistletoe lectin I

Y E R L R L R V T H Q T T G E E Y F R F I
T L L R D Y V S S G S F S N E I P L L R Q
S T I P V S D A Q R F V L V E L T N Q G G
D S I T A A I D V T N L Y V V A Y Q A G D
Q S Y F L R D A P R G A E T H L F T G T T
R S S L P F N G S Y P D L E R Y A G H R D
Q I P L G I D Q L I Q S V T A L R F P G G
S T R T Q A R S I L I L I Q M I S E A A R
F N P I L W R A R Q Y I N S G A S F L P D
V Y M L E L E T S W G Q Q S T Q V Q H S T
D G V F N N P I R L A I P P G N F V T L T
N V R D V I A S L A I M L F V C G E R P S
S S D V R Y W P L V I R P V I A D D V T C
S A S E P T V R I V G R N G M C V D V R D
D D F H D G N Q I Q L W P S K S N N D P N
Q L W T I K R D G T I R S N G S C L T T Y
G Y T A G V Y V M I F D C N T A V R E A T
I W Q I W G N G T I I N P R S N L V L A A
S S G I K G T T L T V Q T L D Y T L G Q G
W L A G N D T A P R E V T I Y G F R D L C
M E S N G G S V W V E T C V S S Q Q N Q R
W A L Y G D G S I R P K Q N Q D Q C L T C
G R D S V S T V I N I V S C S A G S S G Q
R W V F T N E G A I L N L K N G L A M D V
A Q A N P K L R R I I I Y P A T G K P N Q
M W L P V P

Fig. 2a

mistletoe lectin A1

TACGAGAGGCTAAGACTCAGAGTTACGCATCAAACCACGGGCGAGGAATACTTCCGGTTCATC

ACGCTTCTCCGAGATTATGTCTCAAGCGGAAGCTTTTCCAATGAGATACCACTCTTGCGTCAG

TCTACGATCCCCGTCTCCGATGCGCAAAGATTTGTCTTGGTGGAGCTCACCAACCAGGGGCAG

GACTCGGTTACGGCCGCCATCGACGTTACCAATGCTTACGTCGTGGCTTACCAAGCAGGCGAC

CAATCCTACTTTTTGCGCGACGCACCACGCGGCGCGGAAACGCACCTCTTCACCGGCACCACC

CGATCCTCTCTCCCATTCAACGGAAGCTACCCTGATCTGGAGCGATACGCCGGACATAGGGAC

CAGATCCCTCTCGGTATAGACCAACTCATTCAATCCGTCACGGGCGCTTCGTTTTCCGGGCGGC

AGCACGCGTACCCAAGCTCGTTCGATTTTAATCCTCATTCAGATGATCTCCGAGGCCGCCAGA

TTCAATCCCATCTTATGGAGGTACCGCCAATACATTAACAGTGGGGCGTCATTTCTGCCAGAC

GTGTACATGCTGGAGCTGGAGACGAGTTGGGGCCAACAATCCACGCAAGTCCAGCATTCAACC

GATGGCGTTTTTAATAACCCAATTCGGTTGGCTATACCCCCCGGTAACTTCGTGACGTTGACC

AATGTTCGCGACGTGATCGCCAGCTTGGCGATCATGTTGTTTGTATGCGGAGAGCGGCCATCT

TCCTCT

Fig. 2b

mistletoe lectin A1

Y E R L R L R V T H Q T T G E E Y F R F I
T L L R D Y V S S G S F S N E I P L L R Q
S T I P V S D A Q R F V L V E L T N Q G Q
D S V T A A I D V T N A Y V V A Y Q A G D
Q S Y F L R D A P R G A E T H L F T G T T
R S S L P F N G S Y P D L E R Y A G H R D
Q I P L G I D Q L I Q S V T A L R F P G G
S T R T Q A R S I L I L I Q M I S E A A R
F N P I L W R Y R Q Y I N S G A S F L P D
V Y M L E L E T S W G Q Q S T Q V Q H S T
D G V F N N P I R L A I P P G N F V T L T
N V R D V I A S L A I M L F V C G E R P S
S S

Fig. 3a

mistletoe lectin A2

TACGAGAGGCTAAGACTCAGAGTTACGCATCAAACCACGGGCGATGAATACTTCCGGTTCAT

CACGCTTCTCCGAGATTATGTCTCAAGCGGAAGCTTTTCCAATGAGATACCACTCTTGCGTC

AGTCTACGATCCCCGTCTCCGATGCGCAAAGATTTGTCTTGGTGGAGCTCACCAACCAGGGG

CAGGACTCGATCACGGCCGCCATCGACGTTACCAATGCTTACGTCGTGGCTTACCAAGCAGG

CGACCAATCCTACTTTTTGCGCGACGCACCACGCGGCGCGGAAACGCACCTCTTCACCGGCA

CCACCCGAGATAGATCCTCTCTCCCATTCACTGGAAGCTACACCGATCTGGAGCGATACGCC

GGACATAGGGACCAGATCCCTCTCGGTATAGAGCAACTCATTCAATCCGTCTCTGCGCTTCG

TTACCCGGGCGGCAGCACGCGTGCTCAAGCTCGTTCGATTTTAATCCTCATTCAGATGATCT

CCGAGGCCGCCAGATTCAATCCCATCTTATGGAGGTACCGCCAAGATATTAACAGTGGGGAA

TCATTTCTGCCAGACATGTACATGCTGGAGCTGGAGACGAGTTGGGGCCAACAATCCACGCA

AGTCCAGCATTCAACCGATGGCGTTTTTAATAACCCATTCCGGTTGGCTATATCTACTGGTA

ACTTCGTGACGTTGTCTAATGTTCGCTCTGTGATCGCCAGCTTGGCGATCATGTTGTTTGTA

TGCGGAGAGCGGCCATCTTCCTCT

Fig. 3b

mistletoe lectin A2

Y E R L R L R V T H Q T T G D E Y F R F I

T L L R D Y V S S G S F S N E I P L L R Q

S T I P V S D A Q R F V L V E L T N Q G Q

D S I T A A I D V T N A Y V V A Y Q A G D

Q S Y F L R D A P R G A E T H L F T G T T

R D R S S L P F T G S Y T D L E R Y A G H

R D Q I P L G I E Q L I Q S V S A L R Y P

G G S T R A Q A R S I L I L I Q M I S E A

A R F N P I L W R Y R Q D I N S G E S F L

P D M Y M L E L E T S W G Q Q S T Q V Q H

S T D G V F N N P F R L A I S T G N F V T

L S N V R S V I A S L A I M L F V C G E R

P S S S

Fig. 4a

mistletoe lectin I (matched)

TATGAAAGATTGAGGTTGAGGGTGACTCACCAGACTACAGGAGAAGAGTATTTTAGATTTATT

ACTTTGTTGAGGGATTACGTTAGTTCTGGTTCTTTCAGTAACGAAATTCCTTTGCTTAGACAA

TCTACTATTCCAGTTTCTGATGCTCAGCGTTTCGTTCTTGTTGAATTGACTAACCAAGGAGGT

GATAGTATTACTGCTGCTATTGATGTGACTAACCTTTATGTTGTTGCATATCAGGCTGGTGAT

CAGTCTTATTTCCTTAGGGATGCTCCTAGAGGAGCTGAGACTCATTTGTTTACTGGTACAACA

CGGAGTTCTTTGCCTTTTAACGGTTCTTATCCAGACTTGGAAAGATATGCTGGTCACAGAGAT

CAAATTCCATTGGGAATTGATCAGTTGATCCAGAGTGTTACTGCTTTGAGATTCCCAGGTGGA

TCTACTAGAACACAGGCAAGATCTATCCTTATTTTGATCCAAATGATTAGTGAAGCTGCTAGG

TTTAACCCTATTCTTTGGAGAGCAAGACAGTATATCAACTCTGGTGCTTCTTTCCTTCCTGAT

GTTTATATGCTTGAACTTGAAACTTCATGGGGACAGCAGTCTACTCAGGTTCAACACAGTACA

GACGGTGTGTTCAACAATCCTATCAGACTTGCAATTCCACCTGGAAATTTTGTTACTCTTACA

AACGTGAGAGATGTTATTGCTTCTCTTGCTATTATGCTTTTCGTTTGTGGTGAAAGACCTTCT

AGTTCTGATGTTAGATACTGGCCATTGGTTATTAGGCCTGTTATCGCTGACGATGTGACATGT

TCTGCATCTGAACCAACTGTTAGGATCGTTGGAAGAAACGGTATGTGTGTTGATGTTCGGGAC

GATGACTTTCATGACGGTAACCAAATCCAACTTTGGCCTAGTAAGTCTAATAACGACCCAAAC

CAACTTTGGACTATTAAGAGAGACGGTACAATCAGGTCTAACGGATCTTGTCTTACTACATAC

GGTTACACTGCAGGAGTTTACGTTATGATTTTTGATTGCAACACAGCAGTTAGAGAAGCTACA

ATCTGGCAAATCTGGGGTAACGGAACTATTATTAACCCTCGTTCTAACTTGGTGCTTGCTGCT

TCTAGTGGTATTAAGGGAACAACTTTGACTGTTCAGACTTTGGACTATACTCTTGGTCAAGGA

TGGTTGGCTGGAAACGACACAGCTCCTAGAGAAGTTACAATCTACGGATTTAGAGATTTGTGT

ATGGAGTCTAACGGTGGATCTGTTTGGGTTGAAACTTGTGTTTCATCTCAGCAAAATCAGAGG

TGGGCACTTTATGGTGACGGAAGTATCAGACCTAAGCAGAATCAGGATCAGTGTTTGACATGC

GGTAGGGATAGTGTGTCTACTGTTATTAACATTGTGTCTTGTTCTGCAGGTAGTTCTGGACAA

AGGTGGGTTTTCACAAACGAGGGTGCTATCCTTAACTTGAAGAACGGTCTTGCTATGGATGTT

GCTCAGGCTAACCCTAAGTTGAGAAGGATTATCATTTACCCAGCTACTGGTAAGCCTAACCAG

ATGTGGTTGCCAGTTCCTTAT

Fig. 4b

mistletoe lectin I (matched)

Y E R L R L R V T H Q T T G E E Y F R F I

T L L R D Y V S S G S F S N E I P L L R Q

S T I P V S D A Q R F V L V E L T N Q G G

D S I T A A I D V T N L Y V V A Y Q A G D

Q S Y F L R D A P R G A E T H L F T G T T

R S S L P F N G S Y P D L E R Y A G H R D

Q I P L G I D Q L I Q S V T A L R F P G G

S T R T Q A R S I L I L I Q M I S E A A R

F N P I L W R A R Q Y I N S G A S F L P D

V Y M L E L E T S W G Q Q S T Q V Q H S T

D G V F N N P I R L A I P P G N F V T L T

N V R D V I A S L A I M L F V C G E R P S

S S D V R Y W P L V I R P V I A D D V T C

S A S E P T V R I V G R N G M C V D V R D

D D F H D G N Q I Q L W P S K S N N D P N

Q L W T I K R D G T I R S N G S C L T T Y

G Y T A G V Y V M I F D C N T A V R E A T

I W Q I W G N G T I I N P R S N L V L A A

S S G I K G T T L T V Q T L D Y T L G Q G

W L A G N D T A P R E V T I Y G F R D L C

M E S N G G S V W V E T C V S S Q Q N Q R

W A L Y G D G S I R P K Q N Q D Q C L T C

G R D S V S T V I N I V S C S A G S S G Q

R W V F T N E G A I L N L K N G L A M D V

A Q A N P K L R R I I I Y P A T G K P N Q

M W L P V P

Fig. 5a

mistletoe lectin A1 (matched)

TATGAAAGATTGAGGTTGAGGGTGACTCACCAGACTACAGGAGAAGAGTATTTTAGATTTATT

ACTTTGTTGAGGGATTACGTTAGTTCTGGTTCTTTCAGTAACGAAATTCCTTTGCTTAGACAA

TCTACTATTCCAGTTTCTGATGCTCAGCGTTTCGTTCTTGTTGAATTGACTAACCAAGGACAG

GATAGTGTTACTGCTGCTATTGATGTGACTAACGCTTATGTTGTTGCATATCAGGCTGGTGAT

CAGTCTTATTTCCTTAGGGATGCTCCTAGAGGAGCTGAGACTCATTTGTTTACTGGTACAACA

CGGAGTTCTTTGCCTTTTAACGGTTCTTATCCAGACTTGGAAAGATATGCTGGTCACAGAGAT

CAAATTCCATTGGGAATTGATCAGTTGATCCAGAGTGTTACTGCTTTGAGATTCCCAGGTGGA

TCTACTAGAACACAGGCAAGATCTATCCTTATTTTGATCCAAATGATTAGTGAAGCTGCTAGG

TTTAACCCTATTCTTTGGAGATACAGACAGTATATCAACTCTGGTGCTTCTTTCCTTCCTGAT

GTTTATATGCTTGAACTTGAAACTTCATGGGGACAGCAGTCTACTCAGGTTCAACACAGTACA

GACGGTGTGTTCAACAATCCTATCAGACTTGCAATTCCACCTGGAAATTTTGTTACTCTTACA

AACGTGAGAGATGTTATTGCTTCTCTTGCTATTATGCTTTTCGTTTGTGGTGAAAGACCTTCT

AGTTCT

Fig.5b

mistletoe lectin A1 (matched)

Y E R L R L R V T H Q T T G E E Y F R F I

T L L R D Y V S S G S F S N E I P L L R Q

S T I P V S D A Q R F V L V E L T N Q G Q

D S V T A A I D V T N A Y V V A Y Q A G D

Q S Y F L R D A P R G A E T H L F T G T T

R S S L P F N G S Y P D L E R Y A G H R D

Q I P L G I D Q L I Q S V T A L R F P G G

S T R T Q A R S I L I L I Q M I S E A A R

F N P I L W R Y R Q Y I N S G A S F L P D

V Y M L E L E T S W G Q Q S T Q V Q H S T

D G V F N N P I R L A I P P G N F V T L T

N V R D V I A S L A I M L F V C G E R P S

S S

Fig. 6a

mistletoe lectin A2 (matched)

TATGAAAGATTGAGGTTGAGGGTGACTCACCAGACTACAGGAGATGAGTATTTTAGATTTATT

ACTTTGTTGAGGGATTACGTTAGTTCTGGTTCTTTCAGTAACGAAATTCCTTTGCTTAGACAA

TCTACTATTCCAGTTTCTGATGCTCAGCGTTTCGTTCTTGTTGAATTGACTAACCAAGGACAG

GATAGTATTACTGCTGCTATTGATGTGACTAACGCTTATGTTGTTGCATATCAGGCTGGTGAT

CAGTCTTATTTCCTTAGGGATGCTCCTAGAGGAGCTGAGACTCATTTGTTTACTGGTACAACA

CGGGATAGAAGTTCTTTGCCTTTTACTGGTTCTTATACAGACTTGGAAAGATATGCTGGTCAC

AGAGATCAAATTCCATTGGGAATTGAGCAGTTGATCCAGAGTGTTTCTGCTTTGAGATACCCA

GGTGGATCTACTAGAGCTCAGGCAAGATCTATCCTTATTTTGATCCAAATGATTAGTGAAGCT

GCTAGGTTTAACCCTATTCTTTGGAGATACAGACAGGATATCAACTCTGGTGAATCTTTCCTT

CCTGATATGTATATGCTTGAACTTGAAACTTCATGGGGACAGCAGTCTACTCAGGTTCAACAC

AGTACAGACGGTGTGTTCAACAATCCTTTCAGACTTGCAATTTCTACTGGAAATTTTGTTACT

CTTTCTAACGTGAGATCTGTTATTGCTTCTCTTGCTATTATGCTTTTCGTTTGTGGTGAAAGA

CCTTCTAGTTCT

Fig. 6b

mistletoe lectin A2 (matched)

Y E R L R L R V T H Q T T G D E Y F R F I

T L L R D Y V S S G S F S N E I P L L R Q

S T I P V S D A Q R F V L V E L T N Q G Q

D S I T A A I D V T N A Y V V A Y Q A G D

Q S Y F L R D A P R G A E T H L F T G T T

R D R S S L P F T G S Y T D L E R Y A G H

R D Q I P L G I E Q L I Q S V S A L R Y P

G G S T R A Q A R S I L I L I Q M I S E A

A R F N P I L W R Y R Q D I N S G E S F L

P D M Y M L E L E T S W G Q Q S T Q V Q H

S T D G V F N N P F R L A I S T G N F V T

L S N V R S V I A S L A I M L F V C G E R

P S S S

Fig. 7a

mistletoe lectin B

GATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAAATGGCATGTGC

GTGGACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCTCCAAGTCC

AACAATGATCCGAATCAGTTGTGGACGATCAAAAGGGATGGAACCATTCGATCCAATGGCAGC

TGCTTGACCACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTGCT

GTGCGGGAGGCCACTATTTGGCAGATATGGGGCAATGGGACCATCATCAATCCAAGATCCAAT

CTGGTTTTGGCAGCATCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTAC

ACGTTGGGACAGGGCTGGCTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGT

TTCAGGGACCTTTGCATGGAATCAAATGGAGGGAGTGTGTGGGTGGAGACGTGCGTGAGTAGC

CAACAGAACCAAAGATGGGCTTTGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAAGAC

CAATGCCTCACCTGTGGGAGAGACTCCGTTTCAACAGTAATCAATATAGTTAGCTGCAGCGCT

GGATCGTCTGGGCAGCGATGGGTGTTTACCAATGAAGGGGCCATTTTGAATTTAAAGAATGGG

TTGGCCATGGATGTGGCGCAAGCAAATCCAAAGCTCCGCCGAATAATTATCTATCCTGCCACA

GGAAAACCAAATCAAATGTGGCTTCCCGTGCCATGA

Fig. 7b

mistel lectin B

D D V T C S A S E P T V R I V G R N G M C

V D V R D D D F H D G N Q I Q L W P S K S

N N D P N Q L W T I K R D G T I R S N G S

C L T T Y G Y T A G V Y V M I F D C N T A

V R E A T I W Q I W G N G T I I N P R S N

L V L A A S S G I K G T T L T V Q T L D Y

T L G Q G W L A G N D T A P R E V T I Y G

F R D L C M E S N G G S V W V E T C V S S

Q Q N Q R W A L Y G D G S I R P K Q N Q D

Q C L T C G R D S V S T V I N I V S C S A

G S S G Q R W V F T N E G A I L N L K N G

L A M D V A Q A N P K L R R I I I Y P A T

G K P N Q M W L P V P

Fig. 8a

mistletoe lectin B1

GATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAAATGGCATGCGC

GTGGACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCTCCAAGTCC

AACAATGATCCGAATCAGTTGTGGACGATCAAAAGGGATGGAACCATTCGATCCAATGGCAGC

TGCTTGACCACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTGCT

GTGCGGGAGGCCACTATTTGGCAGATATGGGACAATGGGACCATCATCAATCCAAGATCCAAT

CTGGTTTTGGCAGCATCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTAC

ACGTTGGGACAGGGCTGGCTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGT

TTCAGGGACCTTTGCATGGAATCAAATGGAGGGAGTGTGTGGGTGGAGACGTGCGACAGTAGC

CAAAAGAACCAAGGCAAATGGGCTTTGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAA

GACCAATGCCTCACCTCTGGGAGAGACTCCGTTTCAACAGTAATCAATATAGTTAGCTGCAGC

GGAGCTTCGGGGTCTCAGCGATGGGTGTTTACCAATGAAGGGGCCATTTTGAATTTAAAGAAT

GGGTTGGCCATGGATGTGGCGCAAGCAAATCCAAAGCTCCGCCGAATAATTATCTATCCTGCC

ACAGGAAAACCAAATCAAATGTGGCTTCCCGTGTTCTGA

Fig. 8b

mistletoe lectin B1

D D V T C S A S E P T V R I V G R N G M R

V D V R D D D F H D G N Q I Q L W P S K S

N N D P N Q L W T I K R D G T I R S N G S

C L T T Y G Y T A G V Y V M I F D C N T A

V R E A T I W Q I W D N G T I I N P R S N

L V L A A S S G I K G T T L T V Q T L D Y

T L G Q G W L A G N D T A P R E V T I Y G

F R D L C M E S N G G S V W V E T C D S S

Q K N Q G K W A L Y G D G S I R P K Q N Q

D Q C L T S G R D S V S T V I N I V S C S

G A S G S Q R W V F T N E G A I L N L K N

G L A M D V A Q A N P K L R R I I I Y P A

T G K P N Q M W L P V F

Fig. 9a

mistletoe lectin B2

GATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAAGTGGCATGCGC

GTGGACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCTCCAAGTCC

AACAATGATCCGAATCAGTTGTGGACGATCAAAAGGGATAACACCATTCGATCCAATGGCAGC

TGCTTGACCACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTGCT

GTGCGGGAGGCCACTATTTGGCAGATATGGGACAATGGGACCATCATCAATCCAAGATCCAAT

CTGGTTTTGGCAGCATCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTAC

ACGTTGGGACAGGGCTGGCTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGT

TTCAGGGACCTTTGCATGGAATCAAATCAAGGGAGTGTGTGGGTGGAGACGTGCGACAGTAGC

CAAAAGAACCAAGGCAAATGGGCTTTGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAA

GACCAATGCCTCACCGTTGGGAGAGACTCCGTTTCAACAGTAATCAATATAGTTAGCTGCAGC

GGAGCTTCGGGGTCTCAGCGATGGGTGTTTACCAATGAATACGCCATTTTGAATTTAAAGAGT

GGGTTGGCCATGGATGTGGCGCAAGCAAATCCAAAGCTCCGCCGAATAATTATCTATCCTGCC

ACAGGAAAACCAAATCAAATGTGGCTTCCCGTGTTCTGA

Fig. 9b

mistletoe lectin B2

D D V T C S A S E P T V R I V G R S G M R
V D V R D D D F H D G N Q I Q L W P S K S
N N D P N Q L W T I K R D N T I R S N G S
C L T T Y G Y T A G V Y V M I F D C N T A
V R E A T I W Q I W D N G T I I N P R S N
L V L A A S S G I K G T T L T V Q T L D Y
T L G Q G W L A G N D T A P R E V T I Y G
F R D L C M E S N Q G S V W V E T C D S S
Q K N Q G K W A L Y G D G S I R P K Q N Q
D Q C L T V G R D S V S T V I N I V S C S
G A S G S Q R W V F T N E Y A I L N L K S
G L A M D V A Q A N P K L R R I I I Y P A
T G K P N Q M W L P V F

Fig. 10a

mistletoe lectin B3

GATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAAATGGCATGCGC

GTGGACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCTCCAAGTCC

AACAATGATCCGAATCAGTTGTGGACGATCAAAAGGGATGGAACCATTCGATCCAATGGCAGC

TGCTTGACCACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTGCT

GTGCGGGAGGCCACTATTTGGCAGATATGGGACAATGGGACCATCATCAATCCAAGATCCAAT

CTGGTTTTGGCAGCATCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTAC

ACGTTGGGACAGGGCTGGCTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGT

TTCAGGGACCTTTGCATGGAATCAAATGGAGGGAGTGTGTGGGTGGAGACGTGCGACAGTAGC

CAAAAGAACCAAGGCAAATGGGCTTTGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAA

GACCAATGCCTCACCTCTGGGAGAGACTCCGTTTCAACAGTAATCAATATAGTTAGCTGCAGC

GGAGCTTCGGGGTCTCAGCGATGGGTGTTTACCAATGAAGGGGCCATTTTGAATTTAAAGACT

GGGTTGGCCATGGATGTGGCGCAAGCAAATCCAAAGCTCCGCCGAATAATTATCTATCCTGCC

ACAGGAAAACCAAATCAAATGTGGCTTCCCGTGTTCTGA

Fig. 10b

mistletoe lectin B3

D D V T C S A S E P T V R I V G R N G M R

V D V R D D D F H D G N Q I Q L W P S K S

N N D P N Q L W T I K R D G T I R S N G S

C L T T Y G Y T A G V Y V M I F D C N T A

V R E A T I W Q I W D N G T I I N P R S N

L V L A A S S G I K G T T L T V Q T L D Y

T L G Q G W L A G N D T A P R E V T I Y G

F R D L C M E S N G G S V W V E T C D S S

Q K N Q G K W A L Y G D G S I R P K Q N Q

D Q C L T S G R D S V S T V I N I V S C S

G A S G S Q R W V F T N E G A I L N L K T

G L A M D V A Q A N P K L R R I I I Y P A

T G K P N Q M W L P V F

Fig. 11a

mistletoe lectin B4

GATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAAATGGCATGCGC

GTGGACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCTCCAAGTCC

AACAATGATCCGAATCAGTTGTGGACGATCAAAAGGGATGGAACCATTCGATCCAATGGCAGC

TGCTTGACCACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTGCT

GTGCGGGAGGCCACTATTTGGCAGATATGGGACAATGGGACCATCATCAATCCAAGATCCAAT

CTGGTTTTGGCAGCATCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTAC

ACGTTGGGACAGGGCTGGCTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGT

TTCAGGGACCTTTGCATGGAATCAAATGGAGGGAGTGTGTGGGTGGAGACGTGCGACAGTAGC

CAAAAGAACCAAGGCAAATGGGCTTTGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAA

GACCAATGCCTCACCTCTGGGAGAGACTCCGTTTCAACAGTAATCAATATAGTTAGCTGCAGC

GGAGCTTCGGGGTCTCAGCGATGGGTGTTTACCAATGAAGGGGCCATTTTGAATTTAAAGAAA

GGGCCGGCCATGGATGTGGCGCAAGCAAATCCAAAGCTCCGCCGAATAATTATCTATCCTGCC

ACAGGAAAACCAAATCAAATGTGGCTTCCCGTGTTCTGA

Fig. 11b

mistletoe lectin B4

D D V T C S A S E P T V R I V G R N G M R

V D V R D D D F H D G N Q I Q L W P S K S

N N D P N Q L W T I K R D G T I R S N G S

C L T T Y G Y T A G V Y V M I F D C N T A

V R E A T I W Q I W D N G T I I N P R S N

L V L A A S S G I K G T T L T V Q T L D Y

T L G Q G W L A G N D T A P R E V T I Y G

F R D L C M E S N G G S V W V E T C D S S

Q K N Q G K W A L Y G D G S I R P K Q N Q

D Q C L T S G R D S V S T V I N I V S C S

G A S G S Q R W V F T N E G A I L N L K K

G P A M D V A Q A N P K L R R I I I Y P A

T G K P N Q M W L P V F

Fig.12a

mistletoe lectin B5

GATGATGTTACCTGCAGTGCTTCGGAACCTACGGTGCGGATTGTGGGTCGAAATGGCATGCGC

GTGGACGTCCGAGATGACGATTTCCACGATGGGAATCAGATACAGTTGTGGCCCTCCAAGTCC

AACAATGATCCGAATCAGTTGTGGACGATCAAAAGGGATGGAACCATTCGATCCAATGGCAGC

TGCTTGACCACGTATGGCTATACTGCTGGCGTCTATGTGATGATCTTCGACTGTAATACTGCT

GTGCGGGAGGCCACTATTTGGCAGATATGGGACAATGGGACCATCATCAATCCAAGATCCAAT

CTGGTTTTGGCAGCATCATCTGGAATCAAAGGCACTACGCTTACGGTGCAAACACTGGATTAC

ACGTTGGGACAGGGCTGGCTTGCCGGTAATGATACCGCCCCACGCGAGGTGACCATATATGGT

TTCAGGGACCTTTGCATGGAATCAAATGGAGGGAGTGTGTGGGTGGAGACGTGCGACAGTAGC

CAAAAGAACCAAGGCAAATGGGCTTTGTACGGGGATGGTTCTATACGCCCCAAACAAAACCAA

GACCAATGCCTCACCTCTGGGAGAGACTCCGTTTCAACAGTAATCAATATAGTTAGCTGCAGC

GGAGCTTCGGGGTCTCAGCGATGGGTGTTTACCAATGAAGGGGCCATTTTGAATTTAAAGAAT

AGCTTGATGGTGGATGTGGCGCAAGCAAATCCAAAGCTCCGCCGAATAATTATCTATCCTGCC

ACAGGAAAACCAAATCAAATGTGGCTTCCCGTGTTCTGA

Fig. 12b

mistletoe lectin B5

D D V T C S A S E P T V R I V G R N G M R

V D V R D D D F H D G N Q I Q L W P S K S

N N D P N Q L W T I K R D G T I R S N G S

C L T T Y G Y T A G V Y V M I F D C N T A

V R E A T I W Q I W D N G T I I N P R S N

L V L A A S S G I K G T T L T V Q T L D Y

T L G Q G W L A G N D T A P R E V T I Y G

F R D L C M E S N G G S V W V E T C D S S

Q K N Q G K W A L Y G D G S I R P K Q N Q

D Q C L T S G R D S V S T V I N I V S C S

G A S G S Q R W V F T N E G A I L N L K N

S L M V D V A Q A N P K L R R I I I Y P A

T G K P N Q M W L P V F

Fig. 13a

mistletoe lectin B (matched)

GACGATGTGACATGTTCTGCATCTGAACCAACTGTTAGGATCGTTGGAAGAAACGGTATGTGT

GTTGATGTTCGGGACGATGACTTTCATGACGGTAACCAAATCCAACTTTGGCCTAGTAAGTCT

AATAACGACCCAAACCAACTTTGGACTATTAAGAGAGACGGTACAATCAGGTCTAACGGATCT

TGTCTTACTACATACGGTTACACTGCAGGAGTTTACGTTATGATTTTTGATTGCAACACAGCA

GTTAGAGAAGCTACAATCTGGCAAATCTGGGGTAACGGAACTATTATTAACCCTCGTTCTAAC

TTGGTGCTTGCTGCTTCTAGTGGTATTAAGGGAACAACTTTGACTGTTCAGACTTTGGACTAT

ACTCTTGGTCAAGGATGGTTGGCTGGAAACGACACAGCTCCTAGAGAAGTTACAATCTACGGA

TTTAGAGATTTGTGTATGGAGTCTAACGGTGGATCTGTTTGGGTTGAAACTTGTGTTTCATCT

CAGCAAAATCAGAGGTGGGCACTTTATGGTGACGGAAGTATCAGACCTAAGCAGAATCAGGAT

CAGTGTTTGACATGCGGTAGGGATAGTGTGTCTACTGTTATTAACATTGTGTCTTGTTCTGCA

GGTAGTTCTGGACAAAGGTGGGTTTTCACAAACGAGGGTGCTATCCTTAACTTGAAGAACGGT

CTTGCTATGGATGTTGCTCAGGCTAACCCTAAGTTGAGAAGGATTATCATTTACCCAGCTACT

GGTAAGCCTAACCAGATGTGGTTGCCAGTTCCTTAT

Fig. 13b

mistletoe lectin B (matched)

D D V T C S A S E P T V R I V G R N G M C

V D V R D D D F H D G N Q I Q L W P S K S

N N D P N Q L W T I K R D G T I R S N G S

C L T T Y G Y T A G V Y V M I F D C N T A

V R E A T I W Q I W G N G T I I N P R S N

L V L A A S S G I K G T T L T V Q T L D Y

T L G Q G W L A G N D T A P R E V T I Y G

F R D L C M E S N G G S V W V E T C V S S

Q Q N Q R W A L Y G D G S I R P K Q N Q D

Q C L T C G R D S V S T V I N I V S C S A

G S S G Q R W V F T N E G A I L N L K N G

L A M D V A Q A N P K L R R I I I Y P A T

G K P N Q M W L P V P

Fig. 14a

mistletoe lectin (matched)

GACGATGTGACATGTTCTGCATCTGAACCAACTGTTAGGATCGTTGGAAGAAACGGTATGCGT

GTTGATGTTCGGGACGATGACTTTCATGACGGTAACCAAATCCAACTTTGGCCTAGTAAGTCT

AATAACGACCCAAACCAACTTTGGACTATTAAGAGAGACGGTACAATCAGGTCTAACGGATCT

TGTCTTACTACATACGGTTACACTGCAGGAGTTTACGTTATGATTTTTGATTGCAACACAGCA

GTTAGAGAAGCTACAATCTGGCAAATCTGGGATAACGGAACTATTATTAACCCTCGTTCTAAC

TTGGTGCTTGCTGCTTCTAGTGGTATTAAGGGAACAACTTTGACTGTTCAGACTTTGGACTAT

ACTCTTGGTCAAGGATGGTTGGCTGGAAACGACACAGCTCCTAGAGAAGTTACAATCTACGGA

TTTAGAGATTTGTGTATGGAGTCTAACGGTGGATCTGTTTGGGTTGAAACTTGTGATTCATCT

CAGAAAAATCAGGGCAAGTGGGCACTTTATGGTGACGGAAGTATCAGACCTAAGCAGAATCAG

GATCAGTGTTTGACATCCGGTAGGGATAGTGTGTCTACTGTTATTAACATTGTGTCTTGTTCT

GGAGCTAGTGGATCTCAAAGGTGGGTTTTCACAAACGAGGGTGCTATCGTTAACTTGAAGAAC

GGTCTTGCTATGGATGTTGCTCAGGCTAACCCTAAGTTGAGAAGGATTATCATTTACCCAGCT

ACTGGTAAGCCTAACCAGATGTGGTTGCCAGTTTTTTAT

Fig.14b

mistletoe lectin 1 (matched)

D D V T C S A S E P T V R I V G R N G M R

V D V R D D D F H D G N Q I Q L W P S K S

N N D P N Q L W T I K R D G T I R S N G S

C L T T Y G Y T A G V Y V M I F D C N T A

V R E A T I W Q I W D N G T I I N P R S N

L V L A A S S G I K G T T L T V Q T L D Y

T L G Q G W L A G N D T A P R E V T I Y G

F R D L C M E S N G G S V W V E T C D S S

Q K N Q G K W A L Y G D G S I R P K Q N Q

D Q C L T S G R D S V S T V I N I V S C S

G A S G S Q R W V F T N E G A I L N L K N

G L A M D V A Q A N P K L R R I I I Y P A

T G K P N Q M W L P V F

Fig. 15a

mistletoe lectin B2 (matched)

GACGATGTGACATGTTCTGCATCTGAACCAACTGTTAGGATCGTTGGAAGAAGCGGTATGCGT

GTTGATGTTCGGGACGATGACTTTCATGACGGTAACCAAATCCAACTTTGGCCTAGTAAGTCT

AATAACGACCCAAACCAACTTTGGACTATTAAGAGAGACAATACAATCAGGTCTAACGGATCT

TGTCTTACTACATACGGTTACACTGCAGGAGTTTACGTTATGATTTTTGATTGCAACACAGCA

GTTAGAGAAGCTACAATCTGGCAAATCTGGGATAACGGAACTATTATTAACCCTCGTTCTAAC

TTGGTGCTTGCTGCTTCTAGTGGTATTAAGGGAACAACTTTGACTGTTCAGACTTTGGACTAT

ACTCTTGGTCAAGGATGGTTGGCTGGAAACGACACAGCTCCTAGAGAAGTTACAATCTACGGA

TTTAGAGATTTGTGTATGGAGTCTAACCAGGGATCTGTTTGGGTTGAAACTTGTGATTCATCT

CAGAAAAATCAGGGCAAGTGGGCACTTTATGGTGACGGAAGTATCAGACCTAAGCAGAATCAG

GATCAGTGTTTGACAGTCGGTAGGGATAGTGTGTCTACTGTTATTAACATTGTGTCTTGTTCT

GGAGCTAGTGGATCTCAAAGGTGGGTTTTCACAAACGAGTATGCTATCCTTAACTTGAAGTCC

GGTCTTGCTATGGATGTTGCTCAGGCTAACCCTAAGTTGAGAAGGATTATCATTTACCCAGCT

ACTGGTAAGCCTAACCAGATGTGGTTGCCAGTTTTTTAT

Fig. 15b

mistletoe lectin B2 (matched)

D D V T C S A S E P T V R I V G R S G M R

V D V R D D D F H D G N Q I Q L W P S K S

N N D P N Q L W T I K R D N T I R S N G S

C L T T Y G Y T A G V Y V M I F D C N T A

V R E A T I W Q I W D N G T I I N P R S N

L V L A A S S G I K G T T L T V Q T L D Y

T L G Q G W L A G N D T A P R E V T I Y G

F R D L C M E S N Q G S V W V E T C D S S

Q K N Q G K W A L Y G D G S I R P K Q N Q

D Q C L T V G R D S V S T V I N I V S C S

G A S G S Q R W V F T N E Y A I L N L K S

G L A M D V A Q A N P K L R R I I I Y P A

T G K P N Q M W L P V F

Fig.16a

mistletoe lectin B3 (matched)

GACGATGTGACATGTTCTGCATCTGAACCAACTGTTAGGATCGTTGGAAGAAACGGTATGCGT

GTTGATGTTCGGGACGATGACTTTCATGACGGTAACCAAATCCAACTTTGGCCTAGTAAGTCT

AATAACGACCCAAACCAACTTTGGACTATTAAGAGAGACGGTACAATCAGGTCTAACGGATCT

TGTCTTACTACATACGGTTACACTGCAGGAGTTTACGTTATGATTTTTGATTGCAACACAGCA

GTTAGAGAAGCTACAATCTGGCAAATCTGGGATAACGGAACTATTATTAACCCTCGTTCTAAC

TTGGTGCTTGCTGCTTCTAGTGGTATTAAGGGAACAACTTTGACTGTTCAGACTTTGGACTAT

ACTCTTGGTCAAGGATGGTTGGCTGGAAACGACACAGCTCCTAGAGAAGTTACAATCTACGGA

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GGAGCTAGTGGATCTCAAAGGTGGGTTTTCACAAACGAGGGTGCTATCCTTAACTTGAAGACC

GGTCTTGCTATGGATGTTGCTCAGGCTAACCCTAAGTTGAGAAGGATTATCATTTACCCAGCT

ACTGGTAAGCCTAACCAGATGTGGTTGCCAGTTTTTTAT

Fig.16b

mistletoe lectin B3 (matched)

D D V T C S A S E P T V R I V G R N G M R

V D V R D D D F H D G N Q I Q L W P S K S

N N D P N Q L W T I K R D G T I R S N G S

C L T T Y G Y T A G V Y V M I F D C N T A

V R E A T I W Q I W D N G T I I N P R S N

L V L A A S S G I K G T T L T V Q T L D Y

T L G Q G W L A G N D T A P R E V T I Y G

F R D L C M E S N G G S V W V E T C D S S

Q K N Q G K W A L Y G D G S I R P K Q N Q

D Q C L T S G R D S V S T V I N I V S C S

G A S G S Q R W V F T N E G A I L N L K T

G L A M D V A Q A N P K L R R I I I Y P A

T G K P N Q M W L P V F

Fig. 17a

mistletoe lectin B4 (matched)

GACGATGTGACATGTTCTGCATCTGAACCAACTGTTAGGATCGTTGGAAGAAACGGTATGCGT

GTTGATGTTCGGGACGATGACTTTCATGACGGTAACCAAATCCAACTTTGGCCTAGTAAGTCT

AATAACGACCCAAACCAACTTTGGACTATTAAGAGAGACGGTACAATCAGGTCTAACGGATCT

TGTCTTACTACATACGGTTACACTGCAGGAGTTTACGTTATGATTTTTGATTGCAACACAGCA

GTTAGAGAAGCTACAATCTGGCAAATCTGGGATAACGGAACTATTATTAACCCTCGTTCTAAC

TTGGTGCTTGCTGCTTCTAGTGGTATTAAGGGAACAACTTTGACTGTTCAGACTTTGGACTAT

ACTCTTGGTCAAGGATGGTTGGCTGGAAACGACACAGCTCCTAGAGAAGTTACAATCTACGGA

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CAGAAAAATCAGGGCAAGTGGGCACTTTATGGTGACGGAAGTATCAGACCTAAGCAGAATCAG

GATCAGTGTTTGACATCCGGTAGGGATAGTGTGTCTACTGTTATTAACATTGTGTCTTGTTCT

GGAGCTAGTGGATCTCAAAGGTGGGTTTTCACAAACGAGGGTGCTATCCTTAACTTGAAGAAA

GGTCCTGCTATGGATGTTGCTCAGGCTAACCCTAAGTTGAGAAGGATTATCATTTACCCAGCT

ACTGGTAAGCCTAACCAGATGTGGTTGCCAGTTTTTTAT

Fig.17b

mistletoe lectin B4 (matched)

D D V T C S A S E P T V R I V G R N G M R

V D V R D D D F H D G N Q I Q L W P S K S

N N D P N Q L W T I K R D G T I R S N G S

C L T T Y G Y T A G V Y V M I F D C N T A

V R E A T I W Q I W D N G T I I N P R S N

L V L A A S S G I K G T T L T V Q T L D Y

T L G Q G W L A G N D T A P R E V T I Y G

F R D L C M E S N G G S V W V E T C D S S

Q K N Q G K W A L Y G D G S I R P K Q N Q

D Q C L T S G R D S V S T V I N I V S C S

G A S G S Q R W V F T N E G A I L N L K K

G P A M D V A Q A N P K L R R I I I Y P A

T G K P N Q M W L P V F

Fig. 18a

mistletoe lectin B5 (matched)

GACGATGTGACATGTTCTGCATCTGAACCAACTGTTAGGATCGTTGGAAGAAACGGTATGCGT

GTTGATGTTCGGGACGATGACTTTCATGACGGTAACCAAATCCAACTTTGGCCTAGTAAGTCT

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GTTAGAGAAGCTACAATCTGGCAAATCTGGGATAACGGAACTATTATTAACCCTCGTTCTAAC

TTGGTGCTTGCTGCTTCTAGTGGTATTAAGGGAACAACTTTGACTGTTCAGACTTTGGACTAT

ACTCTTGGTCAAGGATGGTTGGCTGGAAACGACACAGCTCCTAGAGAAGTTACAATCTACGGA

TTTAGAGATTTGTGTATGGAGTCTAACGGTGGATCTGTTTGGGTTGAAACTTGTGATTCATCT

CAGAAAAATCAGGGCAAGTGGGCACTTTATGGTGACGGAAGTATCAGACCTAAGCAGAATCAG

GATCAGTGTTTGACATCCGGTAGGGATAGTGTGTCTACTGTTATTAACATTGTGTCTTGTTCT

GGAGCTAGTGGATCTCAAAGGTGGGTTTTCACAAACGAGGGTGCTATCCTTAACTTGAAGAAC

TCTCTTATGGTGGATGTTGCTCAGGCTAACCCTAAGTTGAGAAGGATTATCATTTACCCAGCT

ACTGGTAAGCCTAACCAGATGTGGTTGCCAGTTTTTTAT

Fig.18b

mistletoe lectin B5 (matched)

D	D	V	T	C	S	A	S	E	P	T	V	R	I	V	G	R	N	G	M	R
V	D	V	R	D	D	D	F	H	D	G	N	Q	I	Q	L	W	P	S	K	S
N	N	D	P	N	Q	L	W	T	I	K	R	D	G	T	I	R	S	N	G	S
C	L	T	T	Y	G	Y	T	A	G	V	Y	V	M	I	F	D	C	N	T	A
V	R	E	A	T	I	W	Q	I	W	D	N	G	T	I	I	N	P	R	S	N
L	V	L	A	A	S	S	G	I	K	G	T	T	L	T	V	Q	T	L	D	Y
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F	R	D	L	C	M	E	S	N	G	G	S	V	W	V	E	T	C	D	S	S
Q	K	N	Q	G	K	W	A	L	Y	G	D	G	S	I	R	P	K	Q	N	Q
D	Q	C	L	T	S	G	R	D	S	V	S	T	V	I	N	I	V	S	C	S
G	A	S	G	S	Q	R	W	V	F	T	N	E	G	A	I	L	N	L	K	N
S	L	M	V	D	V	A	Q	A	N	P	K	L	R	R	I	I	I	Y	P	A
T	G	K	P	N	Q	M	W	L	P	V	F									

PA 29 200 US

Atty. Docket No: 29841/36656

DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name; I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled "RECOMBINANT MISTLETOE LECTINS," the specification of which (check one): ☐ is attached hereto; ☒ was filed on August 3, 2000 as Application Serial No. 09/601,667 and was amended on _____ (if applicable); ☐ was filed as PCT International Application No. _____ and was amended under Article 19 on _____ (if applicable). I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment(s) referred to above. I acknowledge the duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined in 37 C.F.R. §1.56.

I hereby claim foreign priority benefits under 35 U.S.C. §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

			Priority Claimed	
198 04 210.8	Germany	03 February 1998	☒ Yes	☐ No
(Application Serial Number)	(Country)	(Day/Month/Year Filed)		
			☐ Yes	☐ No
(Application Serial Number)	(Country)	(Day/Month/Year Filed)		

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below:

(Application Serial Number) (Day/Month/Year Filed)

(Application Serial Number) (Day/Month/Year Filed)

I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s) or PCT international application(s) designating the United States of America listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior application(s) in the manner provided by the first paragraph of 35 U.S.C. §112, I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in 37 C.F.R. §1.56 which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application:

PCT/EP99/00695	05 February 1999	Pending
(Application Serial Number)	(Day/Month/Year Filed)	(Status-Patented, Pending or Abandoned)
(Application Serial Number)	(Day/Month/Year Filed)	(Status-Patented, Pending or Abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: I hereby appoint as my attorneys, with full powers of substitution and revocation, to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

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PATENT & TRADEMARK OFFICE

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        35                  40                  45

Asp Ala Gln Arg Phe Val Leu Val Glu Leu Thr Asn Gln Gly Xaa Asp
    50                  55                  60

Ser Xaa Thr Ala Ala Ile Asp Val Thr Asn Xaa Tyr Val Val Ala Tyr
65                  70                  75                  80

Gln Ala Gly Asp Gln Ser Tyr Phe Leu Arg Asp Ala Pro Arg Gly Ala
                85                  90                  95

Glu Thr His Leu Phe Thr Gly Thr Thr Arg Xaa Ser Ser Leu Pro Phe
            100                 105                 110

Xaa Gly Ser Tyr Xaa Asp Leu Glu Arg Tyr Ala Gly His Arg Asp Gln
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Ile Pro Leu Gly Ile Xaa Gln Leu Ile Gln Ser Val Xaa Ala Leu Arg
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260 265 270

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Asn Leu Lys Xaa Xaa Xaa Xaa Xaa Asp Val Ala Gln Ala Asn Pro Lys
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Leu Arg Arg Ile Ile Ile Tyr Pro Ala Thr Gly Lys Pro Asn Gln Met
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<222>       219
<223>       product= "Xaa is Ile or Phe"
                 /label= Xaa16
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<220>
<221> SITE
<222> 224
<223> product= "Xaa is Pro or Ser"
/label= Xaa17

<220>
<221> SITE
<222> 225
<223> product= "Xaa is Pro or Thr"
/label= Xaa18

<220>
<221> SITE
<222> 232
<223> product= "Xaa is Thr or Ser"
/label= Xaa19

<220>
<221> SITE
<222> 236
<223> product= "Xaa is Asp or Ser"
/label= Xaa20

<400> 2

Tyr Glu Arg Leu Arg Leu Arg Val Thr His Gln Thr Thr Gly Xaa Glu
1 5 10 15

Tyr Phe Arg Phe Ile Thr Leu Leu Arg Asp Tyr Val Ser Ser Gly Ser
20 25 30

Phe Ser Asn Glu Ile Pro Leu Leu Arg Gln Ser Thr Ile Pro Val Ser
35 40 45

Asp Ala Gln Arg Phe Val Leu Val Glu Leu Thr Asn Gln Gly Xaa Asp
50 55 60

Ser Xaa Thr Ala Ala Ile Asp Val Thr Asn Xaa Tyr Val Val Ala Tyr
65 70 75 80

Gln Ala Gly Asp Gln Ser Tyr Phe Leu Arg Asp Ala Pro Arg Gly Ala
85 90 95

Glu Thr His Leu Phe Thr Gly Thr Thr Arg Xaa Ser Ser Leu Pro Phe
100 105 110

Xaa Gly Ser Tyr Xaa Asp Leu Glu Arg Tyr Ala Gly His Arg Asp Gln
115 120 125

Ile Pro Leu Gly Ile Xaa Gln Leu Ile Gln Ser Val Xaa Ala Leu Arg
130 135 140

Xaa Pro Gly Gly Ser Thr Arg Xaa Gln Ala Arg Ser Ile Leu Ile Leu
145 150 155 160

Ile Gln Met Ile Ser Glu Ala Ala Arg Phe Asn Pro Ile Leu Trp Arg
165 170 175

```
Xaa Arg Gln Xaa Ile Asn Ser Gly Xaa Ser Phe Leu Pro Asp Xaa Tyr
                180                 185                 190

Met Leu Glu Leu Glu Thr Ser Trp Gly Gln Gln Ser Thr Gln Val Gln
        195                 200                 205

His Ser Thr Asp Gly Val Phe Asn Asn Pro Xaa Arg Leu Ala Ile Xaa
    210                 215                 220

Xaa Gly Asn Phe Val Thr Leu Xaa Asn Val Arg Xaa Val Ile Ala Ser
225                 230                 235                 240

Leu Ala Ile Met Leu Phe Val Cys Gly Glu Arg Pro Ser Ser Ser
                245                 250                 255
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<210> 3
<211> 264
<212> PRT
<213> Artificial Sequence

<220>
<221> SITE
<222> 18
<223> product= "Xaa is Asn or Ser"
/label= Xaa1

<220>
<221> SITE
<222> 21
<223> product= "Xaa is Cys or Arg"
/label= X2

<220>
<221> SITE
<222> 56
<223> product= "Xaa is Gly or Asn"
/label= Xaa3

<220>
<221> SITE
<222> 95
<223> product= "Xaa is Gly or Asp"
/label= Xaa4

<220>
<221> SITE
<222> 157
<223> product= "Xaa is Gly or Gln"
/label= Xaa5

<220>
<221> SITE
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<223> product= "Xaa is Val or Asp"
/label= Xaa6

<220>

<221> SITE
<222> 170
<223> product= "Xaa is Gln or Lys"
/label= Xaa7

<220>
<221> SITE
<222> 173
<223> product= "Xaa is Gly or missing"
/label= Xaa8

<220>
<221> SITE
<222> 174
<223> product= "Xaa is Arg or Lys"
/label= Xaa9

<220>
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<222> 195
<223> product= "Xaa is Cys or Ser or Val"
/label= Xaa10

<220>
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<222> 211
<223> product= "Xaa is Ala or Gly"
/label= Xaa11

<220>
<221> SITE
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<223> product= "Xaa is Gly or Ala"
/label= Xaa12

<220>
<221> SITE
<222> 214
<223> product= "Xaa is Ser or Gly"
/label= Xaa13

<220>
<221> SITE
<222> 215
<223> product= "Xaa is Gly or Ser"
/label= Xaa14

<220>
<221> SITE
<222> 224
<223> product= "Xaa is Gly or Tyr"
/label= Xaa15

<220>
<221> SITE
<222> 231
<223> product= "Xaa is Asn or Ser or Thr or Lys"
/label= Xaa16

<220>

<221> SITE
<222> 232
<223> product= "Xaa is Ser or Gly"
/label= Xaa17

<220>
<221> SITE
<222> 233
<223> product= "Xaa is Leu or Pro"
/label= Xaa17

<220>
<221> SITE
<222> 234
<223> product= "Xaa is Ala or Met"
/label= Xaa19

<220>
<221> SITE
<222> 235
<223> product= "Xaa is Met or Val"
/label= Xaa20

<220>
<221> SITE
<222> 264
<223> product= "Xaa is Pro or Phe"
/label= Xaa21

<400> 3

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Asp Asp Val Thr Cys Ser Ala Ser Glu Pro Thr Val Arg Ile Val Gly
1               5                  10                  15

Arg Xaa Gly Met Xaa Val Asp Val Arg Asp Asp Asp Phe His Asp Gly
            20                  25                  30

Asn Gln Ile Gln Leu Trp Pro Ser Lys Ser Asn Asn Asp Pro Asn Gln
        35                  40                  45

Leu Trp Thr Ile Lys Arg Asp Xaa Thr Ile Arg Ser Asn Gly Ser Cys
    50                  55                  60

Leu Thr Thr Tyr Gly Tyr Thr Ala Gly Val Tyr Val Met Ile Phe Asp
65                  70                  75                  80

Cys Asn Thr Ala Val Arg Glu Ala Thr Ile Trp Gln Ile Trp Xaa Asn
                85                  90                  95

Gly Thr Ile Ile Asn Pro Arg Ser Asn Leu Val Leu Ala Ala Ser Ser
            100                 105                 110

Gly Ile Lys Gly Thr Thr Leu Thr Val Gln Thr Leu Asp Tyr Thr Leu
        115                 120                 125

Gly Gln Gly Trp Leu Ala Gly Asn Asp Thr Ala Pro Arg Glu Val Thr
    130                 135                 140

Ile Tyr Gly Phe Arg Asp Leu Cys Met Glu Ser Asn Xaa Gly Ser Val
```

```
145                 150                 155                 160

Trp Val Glu Thr Cys Xaa Ser Ser Gln Xaa Asn Gln Xaa Xaa Trp Ala
                165                 170                 175

Leu Tyr Gly Asp Gly Ser Ile Arg Pro Lys Gln Asn Gln Asp Gln Cys
            180                 185                 190

Leu Thr Xaa Gly Arg Asp Ser Val Ser Thr Val Ile Asn Ile Val Ser
        195                 200                 205

Cys Ser Xaa Xaa Ser Xaa Xaa Gln Arg Trp Val Phe Thr Asn Glu Xaa
    210                 215                 220

Ala Ile Leu Asn Leu Lys Xaa Xaa Xaa Xaa Xaa Asp Val Ala Gln Ala
225                 230                 235                 240

Asn Pro Lys Leu Arg Arg Ile Ile Ile Tyr Pro Ala Thr Gly Lys Pro
                245                 250                 255

Asn Gln Met Trp Leu Pro Val Xaa
            260
```

<210> 4
<211> 531
<212> PRT
<213> Artificial Sequence

<400> 4

```
Tyr Glu Arg Leu Arg Leu Arg Val Thr His Gln Thr Thr Gly Glu Glu
1               5                   10                  15

Tyr Phe Arg Phe Ile Thr Leu Leu Arg Asp Tyr Val Ser Ser Gly Ser
            20                  25                  30

Phe Ser Asn Glu Ile Pro Leu Leu Arg Gln Ser Thr Ile Pro Val Ser
        35                  40                  45

Asp Ala Gln Arg Phe Val Leu Val Glu Leu Thr Asn Gln Gly Gly Asp
    50                  55                  60

Ser Ile Thr Ala Ala Ile Asp Val Thr Asn Leu Tyr Val Val Ala Tyr
65                  70                  75                  80

Gln Ala Gly Asp Gln Ser Tyr Phe Leu Arg Asp Ala Pro Arg Gly Ala
                85                  90                  95

Glu Thr His Leu Phe Thr Gly Thr Thr Arg Ser Ser Leu Pro Phe Asn
            100                 105                 110

Gly Ser Tyr Pro Asp Leu Glu Arg Tyr Ala Gly His Arg Asp Gln Ile
        115                 120                 125

Pro Leu Gly Ile Asp Gln Leu Ile Gln Ser Val Thr Ala Leu Arg Phe
    130                 135                 140

Pro Gly Gly Ser Thr Arg Thr Gln Ala Arg Ser Ile Leu Ile Leu Ile
```

145 150 155 160

Gln Met Ile Ser Glu Ala Ala Arg Phe Asn Pro Ile Leu Trp Arg Ala
165 170 175

Arg Gln Tyr Ile Asn Ser Gly Ala Ser Phe Leu Pro Asp Val Tyr Met
180 185 190

Leu Glu Leu Glu Thr Ser Trp Gly Gln Gln Ser Thr Gln Val Gln His
195 200 205

Ser Thr Asp Gly Val Phe Asn Asn Pro Ile Arg Leu Ala Ile Pro Pro
210 215 220

Gly Asn Phe Val Thr Leu Thr Asn Val Arg Asp Val Ile Ala Ser Leu
225 230 235 240

Ala Ile Met Leu Phe Val Cys Gly Glu Arg Pro Ser Ser Ser Asp Val
245 250 255

Arg Tyr Trp Pro Leu Val Ile Arg Pro Val Ile Ala Asp Asp Val Thr
260 265 270

Cys Ser Ala Ser Glu Pro Thr Val Arg Ile Val Gly Arg Asn Gly Met
275 280 285

Cys Val Asp Val Arg Asp Asp Asp Phe His Asp Gly Asn Gln Ile Gln
290 295 300

Leu Trp Pro Ser Lys Ser Asn Asn Asp Pro Asn Gln Leu Trp Thr Ile
305 310 315 320

Lys Arg Asp Gly Thr Ile Arg Ser Asn Gly Ser Cys Leu Thr Thr Tyr
325 330 335

Gly Tyr Thr Ala Gly Val Tyr Val Met Ile Phe Asp Cys Asn Thr Ala
340 345 350

Val Arg Glu Ala Thr Ile Trp Gln Ile Trp Gly Asn Gly Thr Ile Ile
355 360 365

Asn Pro Arg Ser Asn Leu Val Leu Ala Ala Ser Ser Gly Ile Lys Gly
370 375 380

Thr Thr Leu Thr Val Gln Thr Leu Asp Tyr Thr Leu Gly Gln Gly Trp
385 390 395 400

Leu Ala Gly Asn Asp Thr Ala Pro Arg Glu Val Thr Ile Tyr Gly Phe
405 410 415

Arg Asp Leu Cys Met Glu Ser Asn Gly Gly Ser Val Trp Val Glu Thr
420 425 430

Cys Val Ser Ser Gln Gln Asn Gln Arg Trp Ala Leu Tyr Gly Asp Gly
435 440 445

Ser Ile Arg Pro Lys Gln Asn Gln Asp Gln Cys Leu Thr Cys Gly Arg
450 455 460

Asp Ser Val Ser Thr Val Ile Asn Ile Val Ser Cys Ser Ala Gly Ser

```
465                 470                 475                 480

Ser Gly Gln Arg Trp Val Phe Thr Asn Glu Gly Ala Ile Leu Asn Leu
                485                 490                 495

Lys Asn Gly Leu Ala Met Asp Val Ala Gln Ala Asn Pro Lys Leu Arg
            500                 505                 510

Arg Ile Ile Ile Tyr Pro Ala Thr Gly Lys Pro Asn Gln Met Trp Leu
        515                 520                 525

Pro Val Pro
    530
```

<210> 5
<211> 256
<212> PRT
<213> Artificial Sequence

<400> 5

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Tyr Glu Arg Leu Arg Leu Arg Val Thr His Gln Thr Thr Gly Asp Glu
1               5                   10                  15

Tyr Phe Arg Phe Ile Thr Leu Leu Arg Asp Tyr Val Ser Ser Gly Ser
            20                  25                  30

Phe Ser Asn Glu Ile Pro Leu Leu Arg Gln Ser Thr Ile Pro Val Ser
        35                  40                  45

Asp Ala Gln Arg Phe Val Leu Val Glu Leu Thr Asn Gln Gly Gln Asp
    50                  55                  60

Ser Ile Thr Ala Ala Ile Asp Val Thr Asn Ala Tyr Val Val Ala Tyr
65                  70                  75                  80

Gln Ala Gly Asp Gln Ser Tyr Phe Leu Arg Asp Ala Pro Arg Gly Ala
                85                  90                  95

Glu Thr His Leu Phe Thr Gly Thr Thr Arg Asp Arg Ser Ser Leu Pro
            100                 105                 110

Phe Thr Gly Ser Tyr Thr Asp Leu Glu Arg Tyr Ala Gly His Arg Asp
        115                 120                 125

Gln Ile Pro Leu Gly Ile Glu Gln Leu Ile Gln Ser Val Ser Ala Leu
    130                 135                 140

Arg Tyr Pro Gly Gly Ser Thr Arg Ala Gln Ala Arg Ser Ile Leu Ile
145                 150                 155                 160

Leu Ile Gln Met Ile Ser Glu Ala Ala Arg Phe Asn Pro Ile Leu Trp
                165                 170                 175

Arg Tyr Arg Gln Asp Ile Asn Ser Gly Glu Ser Phe Leu Pro Asp Met
            180                 185                 190

Tyr Met Leu Glu Leu Glu Thr Ser Trp Gly Gln Gln Ser Thr Gln Val
```

```
          195                 200                 205

Gln His Ser Thr Asp Gly Val Phe Asn Asn Pro Phe Arg Leu Ala Ile
    210                 215                 220

Ser Thr Gly Asn Phe Val Thr Leu Ser Asn Val Arg Ser Val Ile Ala
225                 230                 235                 240

Ser Leu Ala Ile Met Leu Phe Val Cys Gly Glu Arg Pro Ser Ser Ser
                245                 250                 255
```

<210> 6
<211> 263
<212> PRT
<213> Artificial Sequence

<400> 6

```
Asp Asp Val Thr Cys Ser Ala Ser Glu Pro Thr Val Arg Ile Val Gly
1               5                   10                  15

Arg Asn Gly Met Cys Val Asp Val Arg Asp Asp Asp Phe His Asp Gly
            20                  25                  30

Asn Gln Ile Gln Leu Trp Pro Ser Lys Ser Asn Asn Asp Pro Asn Gln
        35                  40                  45

Leu Trp Thr Ile Lys Arg Asp Gly Thr Ile Arg Ser Asn Gly Ser Cys
    50                  55                  60

Leu Thr Thr Tyr Gly Tyr Thr Ala Gly Val Tyr Val Met Ile Phe Asp
65                  70                  75                  80

Cys Asn Thr Ala Val Arg Glu Ala Thr Ile Trp Gln Ile Trp Gly Asn
                85                  90                  95

Gly Thr Ile Ile Asn Pro Arg Ser Asn Leu Val Leu Ala Ala Ser Ser
            100                 105                 110

Gly Ile Lys Gly Thr Thr Leu Thr Val Gln Thr Leu Asp Tyr Thr Leu
        115                 120                 125

Gly Gln Gly Trp Leu Ala Gly Asn Asp Thr Ala Pro Arg Glu Val Thr
    130                 135                 140

Ile Tyr Gly Phe Arg Asp Leu Cys Met Glu Ser Asn Gly Gly Ser Val
145                 150                 155                 160

Trp Val Glu Thr Cys Val Ser Ser Gln Gln Asn Gln Arg Trp Ala Leu
                165                 170                 175

Tyr Gly Asp Gly Ser Ile Arg Pro Lys Gln Asn Gln Asp Gln Cys Leu
            180                 185                 190

Thr Cys Gly Arg Asp Ser Val Ser Thr Val Ile Asn Ile Val Ser Cys
        195                 200                 205
```

```
Ser Ala Gly Ser Ser Gly Gln Arg Trp Val Phe Thr Asn Glu Gly Ala
    210                 215                 220

Ile Leu Asn Leu Lys Asn Gly Leu Ala Met Asp Val Ala Gln Ala Asn
225                 230                 235                 240

Pro Lys Leu Arg Arg Ile Ile Ile Tyr Pro Ala Thr Gly Lys Pro Asn
                245                 250                 255

Gln Met Trp Leu Pro Val Pro
            260
```

<210> 7
<211> 264
<212> PRT
<213> Artificial Sequence

<400> 7

```
Asp Asp Val Thr Cys Ser Ala Ser Glu Pro Thr Val Arg Ile Val Gly
1               5                   10                  15

Arg Asn Gly Met Arg Val Asp Val Arg Asp Asp Asp Phe His Asp Gly
            20                  25                  30

Asn Gln Ile Gln Leu Trp Pro Ser Lys Ser Asn Asn Asp Pro Asn Gln
        35                  40                  45

Leu Trp Thr Ile Lys Arg Asp Gly Thr Ile Arg Ser Asn Gly Ser Cys
    50                  55                  60

Leu Thr Thr Tyr Gly Tyr Thr Ala Gly Val Tyr Val Met Ile Phe Asp
65                  70                  75                  80

Cys Asn Thr Ala Val Arg Glu Ala Thr Ile Trp Gln Ile Trp Asp Asn
                85                  90                  95

Gly Thr Ile Ile Asn Pro Arg Ser Asn Leu Val Leu Ala Ala Ser Ser
            100                 105                 110

Gly Ile Lys Gly Thr Thr Leu Thr Val Gln Thr Leu Asp Tyr Thr Leu
        115                 120                 125

Gly Gln Gly Trp Leu Ala Gly Asn Asp Thr Ala Pro Arg Glu Val Thr
    130                 135                 140

Ile Tyr Gly Phe Arg Asp Leu Cys Met Glu Ser Asn Gly Gly Ser Val
145                 150                 155                 160

Trp Val Glu Thr Cys Asp Ser Ser Gln Lys Asn Gln Gly Lys Trp Ala
                165                 170                 175

Leu Tyr Gly Asp Gly Ser Ile Arg Pro Lys Gln Asn Gln Asp Gln Cys
            180                 185                 190

Leu Thr Ser Gly Arg Asp Ser Val Ser Thr Val Ile Asn Ile Val Ser
        195                 200                 205
```

Cys Ser Gly Ala Ser Gly Ser Gln Arg Trp Val Phe Thr Asn Glu Gly
210 215 220

Ala Ile Leu Asn Leu Lys Asn Gly Leu Ala Met Asp Val Ala Gln Ala
225 230 235 240

Asn Pro Lys Leu Arg Arg Ile Ile Ile Tyr Pro Ala Thr Gly Lys Pro
245 250 255

Asn Gln Met Trp Leu Pro Val Phe
260

<210> 8
<211> 264
<212> PRT
<213> Artificial Sequence

<400> 8

Asp Asp Val Thr Cys Ser Ala Ser Glu Pro Thr Val Arg Ile Val Gly
1 5 10 15

Arg Ser Gly Met Arg Val Asp Val Arg Asp Asp Asp Phe His Asp Gly
20 25 30

Asn Gln Ile Gln Leu Trp Pro Ser Lys Ser Asn Asn Asp Pro Asn Gln
35 40 45

Leu Trp Thr Ile Lys Arg Asp Asn Thr Ile Arg Ser Asn Gly Ser Cys
50 55 60

Leu Thr Thr Tyr Gly Tyr Thr Ala Gly Val Tyr Val Met Ile Phe Asp
65 70 75 80

Cys Asn Thr Ala Val Arg Glu Ala Thr Ile Trp Gln Ile Trp Asp Asn
85 90 95

Gly Thr Ile Ile Asn Pro Arg Ser Asn Leu Val Leu Ala Ala Ser Ser
100 105 110

Gly Ile Lys Gly Thr Thr Leu Thr Val Gln Thr Leu Asp Tyr Thr Leu
115 120 125

Gly Gln Gly Trp Leu Ala Gly Asn Asp Thr Ala Pro Arg Glu Val Thr
130 135 140

Ile Tyr Gly Phe Arg Asp Leu Cys Met Glu Ser Asn Gln Gly Ser Val
145 150 155 160

Trp Val Glu Thr Cys Asp Ser Ser Gln Lys Asn Gln Gly Lys Trp Ala
165 170 175

Leu Tyr Gly Asp Gly Ser Ile Arg Pro Lys Gln Asn Gln Asp Gln Cys
180 185 190

Leu Thr Val Gly Arg Asp Ser Val Ser Thr Val Ile Asn Ile Val Ser
195 200 205

```
Cys Ser Gly Ala Ser Gly Ser Gln Arg Trp Val Phe Thr Asn Glu Tyr
    210                 215                 220

Ala Ile Leu Asn Leu Lys Ser Gly Leu Ala Met Asp Val Ala Gln Ala
225                 230                 235                 240

Asn Pro Lys Leu Arg Arg Ile Ile Ile Tyr Pro Ala Thr Gly Lys Pro
                245                 250                 255

Asn Gln Met Trp Leu Pro Val Phe
            260
```

<210> 9
<211> 264
<212> PRT
<213> Artificial Sequence

<400> 9

```
Asp Asp Val Thr Cys Ser Ala Ser Glu Pro Thr Val Arg Ile Val Gly
1               5                   10                  15

Arg Asn Gly Met Arg Val Asp Val Arg Asp Asp Asp Phe His Asp Gly
            20                  25                  30

Asn Gln Ile Gln Leu Trp Pro Ser Lys Ser Asn Asn Asp Pro Asn Gln
        35                  40                  45

Leu Trp Thr Ile Lys Arg Asp Gly Thr Ile Arg Ser Asn Gly Ser Cys
    50                  55                  60

Leu Thr Thr Tyr Gly Tyr Thr Ala Gly Val Tyr Val Met Ile Phe Asp
65                  70                  75                  80

Cys Asn Thr Ala Val Arg Glu Ala Thr Ile Trp Gln Ile Trp Asp Asn
                85                  90                  95

Gly Thr Ile Ile Asn Pro Arg Ser Asn Leu Val Leu Ala Ala Ser Ser
            100                 105                 110

Gly Ile Lys Gly Thr Thr Leu Thr Val Gln Thr Leu Asp Tyr Thr Leu
        115                 120                 125

Gly Gln Gly Trp Leu Ala Gly Asn Asp Thr Ala Pro Arg Glu Val Thr
    130                 135                 140

Ile Tyr Gly Phe Arg Asp Leu Cys Met Glu Ser Asn Gly Gly Ser Val
145                 150                 155                 160

Trp Val Glu Thr Cys Asp Ser Ser Gln Lys Asn Gln Gly Lys Trp Ala
                165                 170                 175

Leu Tyr Gly Asp Gly Ser Ile Arg Pro Lys Gln Asn Gln Asp Gln Cys
            180                 185                 190

Leu Thr Ser Gly Arg Asp Ser Val Ser Thr Val Ile Asn Ile Val Ser
        195                 200                 205
```

Cys Ser Gly Ala Ser Gly Ser Gln Arg Trp Val Phe Thr Asn Glu Gly
    210   215   220

Ala Ile Leu Asn Leu Lys Thr Gly Leu Ala Met Asp Val Ala Gln Ala
225   230   235   240

Asn Pro Lys Leu Arg Arg Ile Ile Ile Tyr Pro Ala Thr Gly Lys Pro
                245   250   255

Asn Gln Met Trp Leu Pro Val Phe
            260

<210> 10
<211> 264
<212> PRT
<213> Artificial Sequence

<400> 10

Asp Asp Val Thr Cys Ser Ala Ser Glu Pro Thr Val Arg Ile Val Gly
1   5   10   15

Arg Asn Gly Met Arg Val Asp Val Arg Asp Asp Asp Phe His Asp Gly
            20   25   30

Asn Gln Ile Gln Leu Trp Pro Ser Lys Ser Asn Asn Asp Pro Asn Gln
        35   40   45

Leu Trp Thr Ile Lys Arg Asp Gly Thr Ile Arg Ser Asn Gly Ser Cys
    50   55   60

Leu Thr Thr Tyr Gly Tyr Thr Ala Gly Val Tyr Val Met Ile Phe Asp
65   70   75   80

Cys Asn Thr Ala Val Arg Glu Ala Thr Ile Trp Gln Ile Trp Asp Asn
                85   90   95

Gly Thr Ile Ile Asn Pro Arg Ser Asn Leu Val Leu Ala Ala Ser Ser
            100   105   110

Gly Ile Lys Gly Thr Thr Leu Thr Val Gln Thr Leu Asp Tyr Thr Leu
        115   120   125

Gly Gln Gly Trp Leu Ala Gly Asn Asp Thr Ala Pro Arg Glu Val Thr
    130   135   140

Ile Tyr Gly Phe Arg Asp Leu Cys Met Glu Ser Asn Gly Gly Ser Val
145   150   155   160

Trp Val Glu Thr Cys Asp Ser Ser Gln Lys Asn Gln Gly Lys Trp Ala
                165   170   175

Leu Tyr Gly Asp Gly Ser Ile Arg Pro Lys Gln Asn Gln Asp Gln Cys
            180   185   190

Leu Thr Ser Gly Arg Asp Ser Val Ser Thr Val Ile Asn Ile Val Ser
        195   200   205

Cys Ser Gly Ala Ser Gly Ser Gln Arg Trp Val Phe Thr Asn Glu Gly
    210   215   220

Ala Ile Leu Asn Leu Lys Lys Gly Pro Ala Met Asp Val Ala Gln Ala
225   230   235   240

Asn Pro Lys Leu Arg Arg Ile Ile Ile Tyr Pro Ala Thr Gly Lys Pro
                245   250   255

Asn Gln Met Trp Leu Pro Val Phe
            260

<210> 11
<211> 264
<212> PRT
<213> Artificial Sequence

<400> 11

Asp Asp Val Thr Cys Ser Ala Ser Glu Pro Thr Val Arg Ile Val Gly
1   5   10   15

Arg Asn Gly Met Arg Val Asp Val Arg Asp Asp Asp Phe His Asp Gly
            20   25   30

Asn Gln Ile Gln Leu Trp Pro Ser Lys Ser Asn Asn Asp Pro Asn Gln
        35   40   45

Leu Trp Thr Ile Lys Arg Asp Gly Thr Ile Arg Ser Asn Gly Ser Cys
    50   55   60

Leu Thr Thr Tyr Gly Tyr Thr Ala Gly Val Tyr Val Met Ile Phe Asp
65   70   75   80

Cys Asn Thr Ala Val Arg Glu Ala Thr Ile Trp Gln Ile Trp Asp Asn
                85   90   95

Gly Thr Ile Ile Asn Pro Arg Ser Asn Leu Val Leu Ala Ala Ser Ser
            100   105   110

Gly Ile Lys Gly Thr Thr Leu Thr Val Gln Thr Leu Asp Tyr Thr Leu
        115   120   125

Gly Gln Gly Trp Leu Ala Gly Asn Asp Thr Ala Pro Arg Glu Val Thr
    130   135   140

Ile Tyr Gly Phe Arg Asp Leu Cys Met Glu Ser Asn Gly Gly Ser Val
145   150   155   160

Trp Val Glu Thr Cys Asp Ser Ser Gln Lys Asn Gln Gly Lys Trp Ala
                165   170   175

Leu Tyr Gly Asp Gly Ser Ile Arg Pro Lys Gln Asn Gln Asp Gln Cys
            180   185   190

Leu Thr Ser Gly Arg Asp Ser Val Ser Thr Val Ile Asn Ile Val Ser
        195   200   205

Cys Ser Gly Ala Ser Gly Ser Gln Arg Trp Val Phe Thr Asn Glu Gly
210 215 220

Ala Ile Leu Asn Leu Lys Asn Ser Leu Met Val Asp Val Ala Gln Ala
225 230 235 240

Asn Pro Lys Leu Arg Arg Ile Ile Ile Tyr Pro Ala Thr Gly Lys Pro
245 250 255

Asn Gln Met Trp Leu Pro Val Phe
260

<210> 12
<211> 1598
<212> DNA
<213> Artificial Sequence

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<222> 319
<223> product= "n is gat aga or missing"
/label= Z1

<220>
<221> misc_feature
<222> 1322
<223> product= "n is ggc or missing"
/label= Z2

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cgtcagtcta cgatcccccgt ctccgatgcg caaagatttg tcttggtgga gctcaccaac 180

caggggsrrg actcgrtyac ggccgccatc gacgttacca atsyktacgt cgtggcttac 240

caagcaggcg accaatccta ctttttgcgc gacgcaccac gcggcgcgga aacgcacctc 300

ttcaccggca ccacccgant cctctctccc attcamygga agctacmcyg atctggagcg 360

atacgccgga catagggacc agatccctct cggtatagas caactcattc aatccgtcwc 420

kgcgcttcgt twyccgggcg gcagcacgcg trcycaagct cgttcgattt taatcctcat 480

tcagatgatc tccgaggccg ccagattcaa tcccatctta tggaggkmyc gccaakayat 540

taacagtggg gmrtcatttc tgccagacrt gtacatgctg gagctggaga cgagttgggg 600

ccaacaatcc acgcaagtcc agcattcaac cgatggcgtt tttaataacc cawtycggtt 660

ggctataycy mcyggtaact tcgtgacgtt gwcyaatgtt cgckmygtga tcgccagctt 720

ggcgatcatg ttgtttgtat gcggagagcg gccatcttcc tctgacgtgc gctattggcc 780

gctggtcata cgacccgtga tagccgatga tgttacctgc agtgcttcgg aacctacggt 840

gcggattgtg ggtcgaartg gcatgygcgt ggacgtccga gatgacgatt tccacgatgg 900

gaatcagata cagttgtggc cctccaagtc caacaatgat ccgaatcagt tgtggacgat 960

caaaagggat rrmaccattc gatccaatgg cagctgcttg accacgtatg gctatactgc 1020

tggcgtctat gtgatgatct tcgactgtaa tactgctgtg cgggaggcca ctatttggca 1080

gatatgggrc aatgggacca tcatcaatcc aagatccaat ctggttttgg cagcatcatc 1140

tggaatcaaa ggcactacgc ttacggtgca aacactggat tacacgttgg gacagggctg 1200

gcttgccggt aatgataccg ccccacgcga ggtgaccata tatggtttca gggacctttg 1260

catggaatca aatsraggga gtgtgtgggt ggagacgtgc gwsagtagcc aamagaacca 1320

anaratgggc tttgtacggg gatggttcta tacgccccaa acaaaaccaa gaccaatgcc 1380

tcacckbtgg gagagactcc gtttcaacag taatcaatat agttagctgc agcgswgswt 1440

cgkskkskca gcgatgggtg tttaccaatg aakrsgccat tttgaattta aagavwrgsy 1500

ygrysrtgga tgtggcgcaa gcaaatccaa agctccgccg aataattatc tatcctgcca 1560

caggaaaacc aaatcaaatg tggcttcccg tgyymtga 1598

<210> 13
<211> 763
<212> DNA
<213> Artificial Sequence

<220>
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<222> 319
<223> product= "n is gat aga or missing"
/label= z1

<400> 13

tacgagaggc taagactcag agttacgcat caaaccacgg gcgakgaata cttccggttc 60

atcacgcttc tccgagatta tgtctcaagc ggaagctttt ccaatgagat accactcttg 120

cgtcagtcta cgatccccgt ctccgatgcg caaagatttg tcttggtgga gctcaccaac 180

caggggsrrg actcgrtyac ggccgccatc gacgttacca atsyktacgt cgtggcttac 240

caagcaggcg accaatccta ctttttgcgc gacgcaccac gcggcgcgga aacgcacctc 300

ttcaccggca ccacccgant cctctctccc attcamygga agctacmcyg atctggagcg 360

atacgccgga catagggacc agatccctct cggtatagas caactcattc aatccgtcwc 420

kgcgcttcgt twyccgggcg gcagcacgcg trcycaagct cgttcgattt taatcctcat 480

tcagatgatc tccgaggccg ccagattcaa tcccatctta tggaggkmyc gccaakayat 540

taacagtggg gmrtcatttc tgccagacrt gtacatgctg gagctggaga cgagttgggg 600

ccaacaatcc acgcaagtcc agcattcaac cgatggcgtt tttaataacc cawtycggtt 660

ggctataycy mcyggtaact tcgtgacgtt gwcyaatgtt cgckmygtga tcgccagctt 720

ggcgatcatg ttgtttgtat gcggagagcg gccatcttcc tct 763

<210> 14
<211> 793
<212> DNA
<213> Artificial Sequence

<220>
<221> misc_feature
<222> 517
<223> product= "n is ggc or missing"
/label= Z2

<400> 14

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ygcgtggacg tccgagatga cgatttccac gatgggaatc agatacagtt gtggccctcc 120

aagtccaaca atgatccgaa tcagttgtgg acgatcaaaa gggatrrmac cattcgatcc 180

aatggcagct gcttgaccac gtatggctat actgctggcg tctatgtgat gatcttcgac 240

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aatccaagat ccaatctggt tttggcagca tcatctggaa tcaaaggcac tacgcttacg 360

gtgcaaacac tggattacac gttgggacag ggctggcttg ccggtaatga taccgcccca 420

cgcgaggtga ccatatatgg tttcagggac ctttgcatgg aatcaaatsr agggagtgtg 480

tgggtggaga cgtgcgwsag tagccaamag aaccaanara tgggctttgt acggggatgg 540

ttctatacgc cccaaacaaa accaagacca atgcctcacc kbtgggagag actccgtttc 600

aacagtaatc aatatagtta gctgcagcgs wgswtcgksk kskcagcgat gggtgtttac 660

caatgaakrs gccattttga atttaaagav wrgsyygrys rtggatgtgg cgcaagcaaa 720

tccaaagctc cgccgaataa ttatctatcc tgccacagga aaaccaaatc aaatgtggct 780

tcccgtgyym tga 793

<210> 15
<211> 1596

<212> DNA
<213> Artificial Sequence

<400> 15

tacgagaggc taagactcag agttacgcat caaaccacgg gcgaggaata cttccggttc 60

atcacgcttc tccgagatta tgtctcaagc ggaagctttt ccaatgagat accactcttg 120

cgtcagtcta cgatccccgt ctccgatgcg caaagatttg tcttggtgga gctcaccaac 180

caggggggag actcgatcac ggccgccatc gacgttacca atctgtacgt cgtggcttac 240

caagcaggcg accaatccta ctttttgcgc gacgcaccac gcggcgcgga aacgcacctc 300

ttcaccggca ccacccgatc ctctctccca ttcaacggaa gctaccctga tctggagcga 360

tacgccggac atagggacca gatccctctc ggtatagacc aactcattca atccgtcacg 420

gcgcttcgtt ttccgggcgg cagcacgcgt acccaagctc gttcgatttt aatcctcatt 480

cagatgatct ccgaggccgc cagattcaat cccatcttat ggagggctcg ccaatacatt 540

aacagtgggg cgtcatttct gccagacgtg tacatgctgg agctggagac gagttggggc 600

caacaatcca cgcaagtcca gcattcaacc gatggcgttt ttaataaccc aattcggttg 660

gctatacccc ccggtaactt cgtgacgttg accaatgttc gcgacgtgat cgccagcttg 720

gcgatcatgt tgtttgtatg cggagagcgg ccatcttcct ctgacgtgcg ctattggccg 780

ctggtcatac gacccgtgat agccgatgat gttacctgca gtgcttcgga acctacggtg 840

cggattgtgg gtcgaaatgg catgtgcgtg gacgtccgag atgacgattt ccacgatggg 900

aatcagatac agttgtggcc ctccaagtcc aacaatgatc cgaatcagtt gtggacgatc 960

aaaagggatg gaaccattcg atccaatggc agctgcttga ccacgtatgg ctatactgct 1020

ggcgtctatg tgatgatctt cgactgtaat actgctgtgc gggaggccac tatttggcag 1080

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atggaatcaa atggagggag tgtgtgggtg gagacgtgcg tgagtagcca acagaaccaa 1320

agatgggctt tgtacgggga tggttctata cgccccaaac aaaaccaaga ccaatgcctc 1380

acctgtggga gagactccgt ttcaacagta atcaatatag ttagctgcag cgctggatcg 1440

tctgggcagc gatgggtgtt taccaatgaa ggggccattt tgaatttaaa gaatgggttg 1500

gccatggatg tggcgcaagc aaatccaaag ctccgccgaa taattatcta tcctgccaca 1560

ggaaaaccaa atcaaatgtg gcttcccgtg ccatga 1596

<210> 16
<211> 762
<212> DNA
<213> Artificial Sequence

<400> 16

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atcacgcttc tccgagatta tgtctcaagc ggaagctttt ccaatgagat accactcttg 120

cgtcagtcta cgatccccgt ctccgatgcg caaagatttg tcttggtgga gctcaccaac 180

caggggcagg actcggttac ggccgccatc gacgttacca atgcttacgt cgtggcttac 240

caagcaggcg accaatccta ctttttgcgc gacgcaccac gcggcgcgga aacgcacctc 300

ttcaccggca ccacccgatc ctctctccca ttcaacggaa gctaccctga tctggagcga 360

tacgccggac atagggacca gatccctctc ggtatagacc aactcattca atccgtcacg 420

gcgcttcgtt ttccgggcgg cagcacgcgt acccaagctc gttcgatttt aatcctcatt 480

cagatgatct ccgaggccgc cagattcaat cccatcttat ggaggtaccg ccaatacatt 540

aacagtgggg cgtcatttct gccagacgtg tacatgctgg agctggagac gagttggggc 600

caacaatcca cgcaagtcca gcattcaacc gatggcgttt ttaataaccc aattcggttg 660

gctataaccc ccggtaactt cgtgacgttg accaatgttc gcgacgtgat cgccagcttg 720

gcgatcatgt tgtttgtatg cggagagcgg ccatcttcct ct 762

<210> 17
<211> 768
<212> DNA
<213> Artificial Sequence

<400> 17

tacgagaggc taagactcag agttacgcat caaaccacgg gcgatgaata cttccggttc 60

atcacgcttc tccgagatta tgtctcaagc ggaagctttt ccaatgagat accactcttg 120

cgtcagtcta cgatccccgt ctccgatgcg caaagatttg tcttggtgga gctcaccaac 180

caggggcagg actcgatcac ggccgccatc gacgttacca atgcttacgt cgtggcttac 240

caagcaggcg accaatccta ctttttgcgc gacgcaccac gcggcgcgga aacgcacctc 300

ttcaccggca ccacccgaga tagatcctct ctcccattca ctggaagcta caccgatctg 360

gagcgatacg ccggacatag ggaccagatc cctctcggta tagagcaact cattcaatcc 420

gtctctgcgc ttcgttaccc gggcggcagc acgcgtgctc aagctcgttc gattttaatc 480

ctcattcaga tgatctccga ggccgccaga ttcaatccca tcttatggag gtaccgccaa 540

gatattaaca gtggggaatc atttctgcca gacatgtaca tgctggagct ggagacgagt 600

tggggccaac aatccacgca agtccagcat tcaaccgatg gcgtttttaa taacccattc 660

cggttggcta tatctactgg taacttcgtg acgttgtcta atgttcgctc tgtgatcgcc 720

agcttggcga tcatgttgtt tgtatgcgga gagcggccat cttcctct 768

<210> 18
<211> 1596
<212> DNA
<213> Artificial Sequence

<400> 18

tatgaaagat tgaggttgag ggtgactcac cagactacag gagaagagta ttttagattt 60

attactttgt tgagggatta cgttagttct ggttctttca gtaacgaaat tcctttgctt 120

agacaatcta ctattccagt ttctgatgct cagcgtttcg ttcttgttga attgactaac 180

caaggaggtg atagtattac tgctgctatt gatgtgacta acctttatgt tgttgcatat 240

caggctggtg atcagtctta tttccttagg gatgctccta gaggagctga gactcatttg 300

tttactggta caacacggag ttctttgcct tttaacggtt cttatccaga cttggaaaga 360

tatgctggtc acagagatca aattccattg ggaattgatc agttgatcca gagtgttact 420

gctttgagat tcccaggtgg atctactaga acacaggcaa gatctatcct tattttgatc 480

caaatgatta gtgaagctgc taggtttaac cctattcttt ggagagcaag acagtatatc 540

aactctggtg cttctttcct tcctgatgtt tatatgcttg aacttgaaac ttcatgggga 600

cagcagtcta ctcaggttca acacagtaca gacggtgtgt tcaacaatcc tatcagactt 660

gcaattccac ctggaaattt tgttactctt acaaacgtga gagatgttat tgcttctctt 720

gctattatgc ttttcgtttg tggtgaaaga ccttctagtt ctgatgttag atactggcca 780

ttggttatta ggcctgttat cgctgacgat gtgacatgtt ctgcatctga accaactgtt 840

aggatcgttg gaagaaacgg tatgtgtgtt gatgttcggg acgatgactt tcatgacggt 900

aaccaaatcc aactttggcc tagtaagtct aataacgacc caaaccaact ttggactatt 960

aagagagacg gtacaatcag gtctaacgga tcttgtctta ctacatacgg ttacactgca 1020

ggagtttacg ttatgatttt tgattgcaac acagcagtta gagaagctac aatctggcaa 1080

atctggggta acggaactat tattaaccct cgttctaact tggtgcttgc tgcttctagt 1140

ggtattaagg gaacaacttt gactgttcag actttggact atactcttgg tcaaggatgg 1200

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tctggacaaa ggtgggtttt cacaaacgag ggtgctatcc ttaacttgaa gaacggtctt 1500

gctatggatg ttgctcaggc taaccctaag ttgagaagga ttatcattta cccagctact 1560

ggtaagccta accagatgtg gttgccagtt ccttat 1596

<210> 19
<211> 762
<212> DNA
<213> Artificial Sequence

<400> 19

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attactttgt tgagggatta cgttagttct ggttctttca gtaacgaaat tcctttgctt 120

agacaatcta ctattccagt ttctgatgct cagcgtttcg ttcttgttga attgactaac 180

caaggacagg atagtgttac tgctgctatt gatgtgacta acgcttatgt tgttgcatat 240

caggctggtg atcagtctta tttccttagg gatgctccta gaggagctga gactcatttg 300

tttactggta caacacggag ttctttgcct tttaacggtt cttatccaga cttggaaaga 360

tatgctggtc acagagatca aattccattg ggaattgatc agttgatcca gagtgttact 420

gctttgagat tcccaggtgg atctactaga acacaggcaa gatctatcct tattttgatc 480

caaatgatta gtgaagctgc taggtttaac cctattcttt ggagatacag acagtatatc 540

aactctggtg cttctttcct tcctgatgtt tatatgcttg aacttgaaac ttcatgggga 600

cagcagtcta ctcaggttca acacagtaca gacggtgtgt tcaacaatcc tatcagactt 660

gcaattccac ctggaaattt tgttactctt acaaacgtga gagatgttat tgcttctctt 720

gctattatgc ttttcgtttg tggtgaaaga ccttctagtt ct 762

<210> 20
<211> 768
<212> DNA
<213> Artificial Sequence

<400> 20

tatgaaagat tgaggttgag ggtgactcac cagactacag gagatgagta ttttagattt 60

attactttgt tgagggatta cgttagttct ggttctttca gtaacgaaat tcctttgctt 120

agacaatcta ctattccagt ttctgatgct cagcgtttcg ttcttgttga attgactaac 180

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gtttctgctt tgagataccc aggtggatct actagagctc aggcaagatc tatccttatt 480

ttgatccaaa tgattagtga agctgctagg tttaacccta ttctttggag atacagacag 540

gatatcaact ctggtgaatc tttccttcct gatatgtata tgcttgaact tgaaacttca 600

tggggacagc agtctactca ggttcaacac agtacagacg gtgtgttcaa caatcctttc 660

agacttgcaa tttctactgg aaatttttgtt actctttcta acgtgagatc tgttattgct 720

tctcttgcta ttatgctttt cgtttgtggt gaaagacctt ctagttct 768

<210> 21
<211> 792
<212> DNA
<213> Artificial Sequence

<400> 21

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tgcgtggacg tccgagatga cgatttccac gatgggaatc agatacagtt gtggccctcc 120

aagtccaaca atgatccgaa tcagttgtgg acgatcaaaa gggatggaac cattcgatcc 180

aatggcagct gcttgaccac gtatggctat actgctggcg tctatgtgat gatcttcgac 240

tgtaatactg ctgtgcggga ggccactatt tggcagatat ggggcaatgg gaccatcatc 300

aatccaagat ccaatctggt tttggcagca tcatctggaa tcaaaggcac tacgcttacg 360

gtgcaaacac tggattacac gttgggacag ggctggcttg ccggtaatga taccgcccca 420

cgcgaggtga ccatatatgg tttcagggac ctttgcatgg aatcaaatgg agggagtgtg 480

tgggtggaga cgtgcgtgag tagccaacag aaccaaagat gggctttgta cggggatggt 540

tctatacgcc ccaaacaaaa ccaagaccaa tgcctcacct gtgggagaga ctccgtttca 600

acagtaatca atatagttag ctgcagcgct ggatcgtctg ggcagcgatg ggtgtttacc 660

aatgaagggg ccattttgaa tttaaagaat gggttggcca tggatgtggc gcaagcaaat 720

ccaaagctcc gccgaataat tatctatcct gccacaggaa aaccaaatca aatgtggctt 780

cccgtgccat ga 792

<210> 22
<211> 795
<212> DNA
<213> Artificial Sequence

<400> 22

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cgcgtggacg tccgagatga cgatttccac gatgggaatc agatacagtt gtggccctcc 120

aagtccaaca atgatccgaa tcagttgtgg acgatcaaaa gggatggaac cattcgatcc 180

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cgcgaggtga ccatatatgg tttcagggac ctttgcatgg aatcaaatgg agggagtgtg 480

tgggtggaga cgtgcgacag tagccaaaag aaccaaggca aatgggcttt gtacggggat 540

ggttctatac gccccaaaca aaaccaagac caatgcctca cctctgggag agactccgtt 600

tcaacagtaa tcaatatagt tagctgcagc ggagcttcgg ggtctcagcg atgggtgttt 660

accaatgaag gggccatttt gaatttaaag aatgggttgg ccatggatgt ggcgcaagca 720

aatccaaagc tccgccgaat aattatctat cctgccacag gaaaaccaaa tcaaatgtgg 780

cttcccgtgt tctga 795

<210> 23
<211> 795
<212> DNA
<213> Artificial Sequence

<400> 23

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cgcgtggacg tccgagatga cgatttccac gatgggaatc agatacagtt gtggccctcc 120

aagtccaaca atgatccgaa tcagttgtgg acgatcaaaa gggataacac cattcgatcc 180

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gtgcaaacac tggattacac gttgggacag ggctggcttg ccggtaatga taccgcccca 420

cgcgaggtga ccatatatgg tttcagggac ctttgcatgg aatcaaatca agggagtgtg 480

tgggtggaga cgtgcgacag tagccaaaag aaccaaggca aatgggcttt gtacggggat 540

ggttctatac gccccaaaca aaaccaagac caatgcctca ccgttgggag agactccgtt 600

tcaacagtaa tcaatatagt tagctgcagc ggagcttcgg ggtctcagcg atgggtgttt 660

accaatgaat acgccatttt gaatttaaag agtgggttgg ccatggatgt ggcgcaagca 720

aatccaaagc tccgccgaat aattatctat cctgccacag gaaaaccaaa tcaaatgtgg 780

cttcccgtgt tctga 795

<210> 24
<211> 795
<212> DNA
<213> Artificial Sequence

<400> 24

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cgcgtggacg tccgagatga cgatttccac gatgggaatc agatacagtt gtggccctcc 120

aagtccaaca atgatccgaa tcagttgtgg acgatcaaaa gggatggaac cattcgatcc 180

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gtgcaaacac tggattacac gttgggacag ggctggcttg ccggtaatga taccgcccca 420

cgcgaggtga ccatatatgg tttcagggac ctttgcatgg aatcaaatgg agggagtgtg 480

tgggtggaga cgtgcgacag tagccaaaag aaccaaggca aatgggcttt gtacggggat 540

ggttctatac gccccaaaca aaaccaagac caatgcctca cctctgggag agactccgtt 600

tcaacagtaa tcaatatagt tagctgcagc ggagcttcgg ggtctcagcg atgggtgttt 660

accaatgaag ggccatttt gaatttaaag actgggttgg ccatggatgt ggcgcaagca 720

aatccaaagc tccgccgaat aattatctat cctgccacag gaaaaccaaa tcaaatgtgg 780

cttcccgtgt tctga 795

<210> 25
<211> 795
<212> DNA
<213> Artificial Sequence

<400> 25

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cgcgtggacg tccgagatga cgatttccac gatgggaatc agatacagtt gtggccctcc 120

aagtccaaca atgatccgaa tcagttgtgg acgatcaaaa gggatggaac cattcgatcc 180

aatggcagct gcttgaccac gtatggctat actgctggcg tctatgtgat gatcttcgac 240

tgtaatactg ctgtgcggga ggccactatt tggcagatat gggacaatgg gaccatcatc 300

aatccaagat ccaatctggt tttggcagca tcatctggaa tcaaaggcac tacgcttacg 360

gtgcaaacac tggattacac gttgggacag ggctggcttg ccggtaatga taccgcccca 420

cgcgaggtga ccatatatgg tttcagggac ctttgcatgg aatcaaatgg agggagtgtg 480

tgggtggaga cgtgcgacag tagccaaaag aaccaaggca aatgggcttt gtacggggat 540

ggttctatac gccccaaaca aaaccaagac caatgcctca cctctgggag agactccgtt 600

tcaacagtaa tcaatatagt tagctgcagc ggagcttcgg ggtctcagcg atgggtgttt 660

accaatgaag ggccatttt gaatttaaag aaagggccgg ccatggatgt ggcgcaagca 720

aatccaaagc tccgccgaat aattatctat cctgccacag gaaaaccaaa tcaaatgtgg 780

cttcccgtgt tctga 795

<210> 26
<211> 795
<212> DNA
<213> Artificial Sequence

<400> 26

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cgcgtggacg tccgagatga cgatttccac gatgggaatc agatacagtt gtggccctcc 120

aagtccaaca atgatccgaa tcagttgtgg acgatcaaaa gggatggaac cattcgatcc 180

aatggcagct gcttgaccac gtatggctat actgctggcg tctatgtgat gatcttcgac 240

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cgcgaggtga ccatatatgg tttcagggac ctttgcatgg aatcaaatgg agggagtgtg 480

tgggtggaga cgtgcgacag tagccaaaag aaccaaggca aatgggcttt gtacggggat 540

ggttctatac gccccaaaca aaaccaagac caatgcctca cctctgggag agactccgtt 600

tcaacagtaa tcaatatagt tagctgcagc ggagcttcgg ggtctcagcg atgggtgttt 660

accaatgaag ggccatttt gaatttaaag aatagcttga tggtggatgt ggcgcaagca 720

aatccaaagc tccgccgaat aattatctat cctgccacag gaaaaccaaa tcaaatgtgg 780

cttcccgtgt tctga 795

<210> 27
<211> 792
<212> DNA
<213> Artificial Sequence

<400> 27

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tgtgttgatg ttcgggacga tgactttcat gacggtaacc aaatccaact ttggcctagt 120

aagtctaata acgacccaaa ccaactttgg actattaaga gagacggtac aatcaggtct 180

aacggatctt gtcttactac atacggttac actgcaggag tttacgttat gatttttgat 240

tgcaacacag cagttagaga agctacaatc tggcaaatct ggggtaacgg aactattatt 300

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gttcagactt tggactatac tcttggtcaa ggatggttgg ctggaaacga cacagctcct 420

agagaagtta caatctacgg atttagagat ttgtgtatgg agtctaacgg tggatctgtt 480

tgggttgaaa cttgtgtttc atctcagcaa aatcagaggt gggcacttta tggtgacgga 540

agtatcagac ctaagcagaa tcaggatcag tgtttgacat gcggtaggga tagtgtgtct 600

actgttatta acattgtgtc ttgttctgca ggtagttctg gacaaaggtg ggttttcaca 660

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Summary

Recombinant Mistletoe Lectins

The present invention relates to processes for the production of mistletoe lectin polypeptides in homologous and heterologous host systems and mistletoe lectin peptides as such. Further, nucleic acid molecules are provided, which code for these mistletoe lectin polypeptides, and also pharmaceutical compositions which contain these mistletoe lectin polypeptides or mistletoe lectin nucleic acids.

In order to produce the many mistletoe lectin isoenzymes contained in the natural mistletoe extract, which can trigger anti-tumorigenic and mood-brightening effects, in sufficient quantities, the present invention provides a process which makes it possible to produce mistletoe lectins in required quantities biotechnologically and at the same time to recreate the diversity of the natural mistletoe extract in mistletoe lectin isoenzymes.